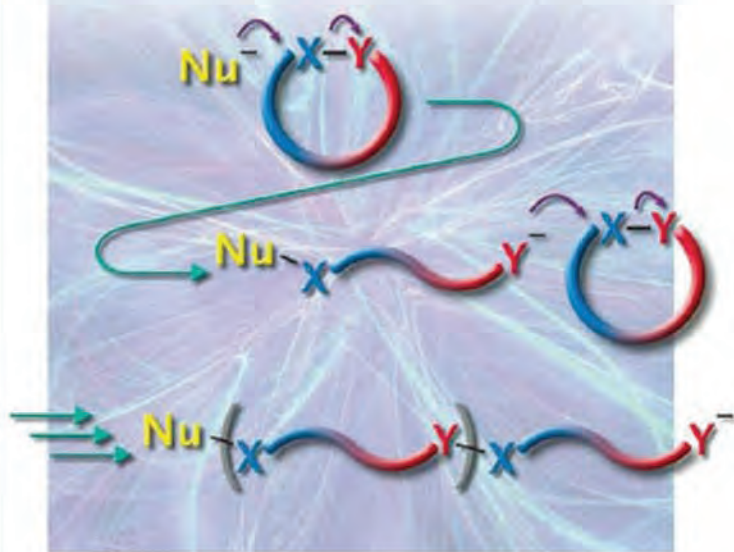


Philippe Dubois, Olivier Coulembier
and Jean-Marie Raquez (Eds.)

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Handbook of Ring-Opening Polymerization



Handbook of Ring-Opening Polymerization

Edited by
Philippe Dubois, Olivier Coulembier, and
Jean-Marie Raquez



WILEY-VCH Verlag GmbH & Co. KGaA

**Handbook of Ring-Opening
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*Edited by
Philippe Dubois,
Olivier Coulembier, and
Jean-Marie Raquez*

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Philippe Dubois, Olivier Coulembier, and
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Preface

Nowadays, polymeric materials—which we commonly refer to as ‘plastics’—form part of our daily life, finding applications in areas as diverse and versatile as automobiles, textiles, building construction and furniture, medicines, pharmacy, electric and electronic devices, and packaging. Among the vast worldwide production of synthetic ‘plastics’—which today is estimated at over 200 million metric tons per year—the so-called ‘commodity polymers’, including polyolefins such as polyethylene and polypropylene (and their derivatives), polyvinylchloride and styrene-based (co)polymers, undoubtedly share the major sector of the market in terms of volume production. All of these are cheap materials with physico-chemical and thermo-mechanical properties that allow their adaptation to a wide range of low-cost uses. For other, more demanding and specific applications, however, higher-performing synthetic polymeric materials are required, and this is where the ‘engineering plastics’ find their greatest use. Although produced in (relatively) smaller volumes, this family of polymeric materials today attracts interest over an enormous range of valuable applications.

Polymers and copolymers obtained by the ring-opening polymerization (ROP) process today constitute a significant portion of the ‘engineering plastics’ industry, where they are mainly used in the preparation of specialty materials. Among the many polymers produced by ROP, one example worthy of highlight is Nylon®-6, a polyamide produced via ring-opening of the ϵ -caprolactam monomer. Although the first reports of the polymerization of lactams date back over 70 years, many of the fine details of the mechanism and kinetics involved still remain unanswered today. Consequently, in recent years many new reaction pathways have been investigated and a range of new catalytic processes developed that allow for the production of new copolymers, either between different lactams themselves, or between lactams and other (cyclic) monomers such as lactones. In the future, ROP will clearly pave the way to the creation of novel, high-performing materials, the properties of which may be tunable so that the (co)polymerization reaction can be controlled to a significant degree.

This *Handbook of Ring-Opening Polymerization* is intended as a single comprehensive reference covering all main classes of monomers, including heterocyclics, cyclic olefins and alkynes, and cycloalkanes, with special emphasis on the polymerization tools required for the precise control of macromolecular parameters,

structure and properties, and on the design of materials of practical interest. It is hoped that the Handbook will serve as a source of information for students, research teams, professors and technologists alike, as well as industrial managers. It thus aims to provide an integrated view of the various areas of research and to identify current trends in ROP.

All of the chapters in this *Handbook of Ring-Opening Polymerization* have been written by internationally recognized experts in their field and, for ease of reading, have been allocated to three parts.

Part 1 covers the theory and fundamentals of ROP, where Chapter 1 describes the thermodynamics and kinetics of the process, and Chapter 2 provides a description of the general mechanisms involved.

Part 2 includes chapters on specific classes of cyclic monomers and their polymerization mechanisms and kinetics, their main (co)polymer architectures and related products, as well as current and future applications. Hence, siloxane-containing and sulfur–nitrogen–phosphorus-containing polymers are described in Chapters 3 and 4, respectively, while the polymerization of cyclic depsipeptides, ureas and urethanes, of polyethers and polyoxazolines, and of polyamides are detailed in Chapters 5, 6 and 7, respectively. Chapters 9, 10, 11 and 12 include details of polyesters prepared from either β -lactones, from dilactones, from larger lactones and from polycarbonates, while the polymerization of cycloalkanes is described in Chapter 13. It should be noted that, slightly ‘out of place’, Chapter 8 covers the subject of ring-opening metathesis polymerization.

Part 3 is devoted more to the implementation of ‘green chemistry’ in ROP processes, where the latest advances in metal-free catalysis in ROP are described in Chapter 14, and of enzyme-mediated ROP in Chapter 15.

In preparing this Handbook, the efforts of all authors in providing up-to-date accounts of their research and development activities in the field of ROP are greatly appreciated. Grateful thanks are also extended to Dr Philippe Degée (who is now working at Cabot International, Belgium) for his extreme help not only in the initial launch of this Handbook but also for the valuable advice that he provided during its creation.

Mons, Belgium, November 2007

Philippe Dubois

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1

Thermodynamics and Kinetics of Ring-Opening Polymerization

Andrzej Duda and Adam Kowalski

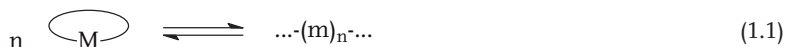
1.1

Introduction

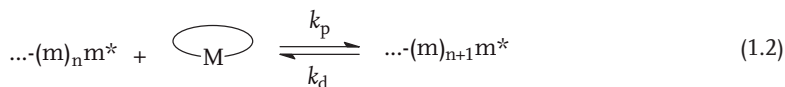
Cyclic monomers that have been polymerized via ring-opening encompass a variety of structures, such as alkanes, alkenes, compounds containing heteroatoms in the ring: oxygen [ethers, acetals, esters (lactones, lactides, and carbonates), and anhydrides], sulfur (polysulfur, sulfides and polysulfides), nitrogen [amines, amides (lactams), imides, *N*-carboxyanhydrides and 1,3-oxaza derivatives], phosphorus (phosphates, phosphonates, phosphites, phosphines and phosphazenes), or silicon (siloxanes, silaethers, carbosilanes and silanes). For the majority of these monomers, convenient polymerization conditions have been elaborated, that result in the controlled synthesis of the corresponding polymers [1–13].

The ability of a cyclic monomer to polymerize according to the ring-opening mechanism is determined by two equally important factors—the conversion of monomer molecules into macromolecules (of linear or more complex topologies) must be allowed both thermodynamically and kinetically. In practical terms this means that: (i) monomer-macromolecule equilibrium must be shifted to the right-hand (macromolecule) side; and (ii) the corresponding polymerization mechanism should exist, that could enable conversion of the monomer molecules into the polymer repeating units, within the operable polymerization time (Equation 1.1).

The net equation of the polymerization process reads:



where M denotes the monomer molecule, and m is the macromolecule repeating unit derived from the M monomer; whereas an elementary reaction of the macromolecular chain growth can be written as:

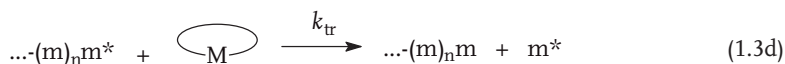
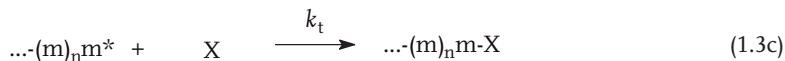
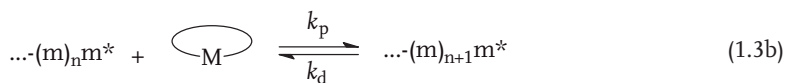
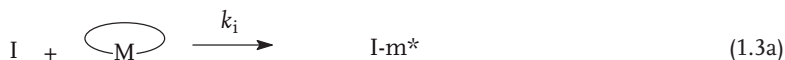


where m^* denotes the active species, and k_p and k_d are the rate constants of propagation and depropagation, respectively.

Depending on the monomer and catalytic/initiating system and the nature of the resulting active species, a number of mechanisms can operate in the ring-opening polymerization (ROP). The mechanisms most often employed include coordination, covalent, ionic (anionic or cationic), metathetic, radical and enzymatic. With regards to location of the active species, active chain-end or activated monomer mechanisms can be distinguished. A more detailed discussion of the ROP mechanisms is presented in Chapter 2.

In contrast to the polymerization of a large majority of unsaturated monomers, the ROP of cyclic monomers is often accompanied by the presence of a relatively high concentration of the unreacted monomer when the process comes to equilibrium. This feature is related to a pronounced reversibility of the propagation step (i.e. relatively high k_d in comparison to k_p ; Equation 1.2). Thus, a value of the equilibrium monomer concentration ($[M]_{eq}$) is usually taken as a measure of the monomer thermodynamic polymerizability. The corresponding thermodynamic formalism was developed by Dainton and Ivin in 1948 [14, 15], and subsequently by Tobolsky and Eisenberg [16, 17].

The reaction of a monomer with initiating agents (Equation 1.3a) should lead to active species capable of adding new monomer molecules (Equation 1.3b); moreover, they should be added faster than they undergo any side reactions, such as termination (Equation 1.3c) or transfer to monomer (Equation 1.3d).



where I denotes the initiator molecule, m^* is the active species, X is the terminating agent, and k_p , k_d , k_t , k_{tr} are the rate constants of propagation, depropagation, termination and transfer, respectively.

For an idealized, living polymerization: $k_t = 0$ and $k_{tr} = 0$. A discovery of the anionic living polymerization of vinyl and diene monomers by Szwarc and coworkers opened a new chapter in macromolecular science [18–20]. ROP, being the subject of the present chapter, may also proceed as a living process. However, molar mass and end group control of the resultant polymer is only possible when $k_i \geq k_p$ (Equations 1.3a and 1.3b).

As both the thermodynamics [2, 7, 8, 21–27] and kinetics [1–4, 6–8, 10, 12] of ROP have been reviewed extensively in the past, this chapter provides a concise description of only the most important and general phenomena.

1.2

Thermodynamics of the Ring-Opening Polymerization

1.2.1

Equilibrium Monomer Concentration: Ceiling/Floor Temperatures

The formal thermodynamic criterion of a given monomer polymerizability is related to a sign of the free enthalpy (called also Gibbs energy) of polymerization (cf. Equation 1.1):

$$\Delta G_p(xy) = \Delta H_p(xy) - T\Delta S_p(xy) \quad (1.4)$$

where x and y denote monomer and polymer states, respectively [i.e.: x and/or $y = l$ (liquid), g (gaseous), c (solid amorphous), c' (solid crystalline), s (solution)], $\Delta H_p(xy)$ and $\Delta S_p(xy)$ are the corresponding enthalpy and entropy of polymerization, and T is the absolute temperature.

In agreement with the general rules of the thermodynamics of chemical processes, only when $\Delta G_p(xy) < 0$ is polymerization possible. It must be stressed, however, that the $\Delta G_p(xy)$ values usually depend on the monomer and polymer states. Even in solution, polymerization $\Delta G_p(xy)$ may depend on the solvent used (see Section 1.2.2.2). Further analysis, if not otherwise indicated, will be related to ROP carried out in solution or in the monomer/polymer melt and under the constant temperature and pressure.

The free enthalpy of polymerization (ΔG_p) may be expressed as a sum of standard enthalpy of polymerization (ΔG_p°) and a term related to instantaneous monomer molecules and growing macromolecules concentrations:

$$\Delta G_p = \Delta G_p^\circ + RT \ln \frac{[\dots(m)_{i+1}m^*]}{[M][\dots(m)_im^*]} \quad (1.5)$$

where R denotes the gas constant.

Following Flory's assumption that the reactivity of an active center, located at a macromolecule of a sufficiently long macromolecular chain, does not depend on its polymerization degree (DP_i), and taking into account that $\Delta G_p^\circ = \Delta H_p^\circ - T\Delta S_p^\circ$ (where ΔH_p° and ΔS_p° denote a standard polymerization enthalpy and entropy, respectively), we obtain:

$$\Delta G_p = \Delta H_p^\circ - T(\Delta S_p^\circ + R \ln[M]) \quad (1.6)$$

At equilibrium ($\Delta G_p = 0$)—that is, when polymerization is complete the monomer concentration ($[M]_{eq}$) assumes a value determined by standard polymerization parameters (ΔH_p° and ΔS_p°) and polymerization temperature (see e.g. Refs. [10, 14–17, 21–26]):

$$\ln[M]_{eq} = \Delta H_p^\circ / RT - \Delta S_p^\circ / R \quad (1.7a)$$

$$[M]_{eq} = \exp(\Delta H_p^\circ / RT - \Delta S_p^\circ / R) \quad (1.7b)$$

Depending on the starting monomer concentration ($[M]_0$), or actually on the $([M]_0 - [M]_{eq}) / \sum [\dots m_i^*]$ ratio, polymers of various number average polymerization degrees (DP_n) may be formed. Thus, polymerization is possible only when $[M]_0 > [M]_{eq}$. For shorter, oligomeric chains (approximately $DP_n \leq 20$) that do not conform to the Flory's assumption, in the expressions for $[M]_{eq}$ the value of DP_n has to be taken into account (see Appendix in Ref. [28]):

$$\ln\left(\frac{DP_n}{DP_n - 1} [M]_{eq}\right) = \frac{\Delta H_p^\circ}{RT} - \frac{\Delta S_p^\circ}{R} \quad (1.8a)$$

$$[M]_{eq} = \frac{DP_n - 1}{DP_n} \exp\left(\frac{\Delta H_p^\circ}{RT} - \frac{\Delta S_p^\circ}{R}\right) \quad (1.8b)$$

Figure 1.1 shows an example of applying Equation 1.8a to a determination of the standard thermodynamic parameters in the ROP of 1,4-dioxane-2-one (DX) using the experimentally determined $[M]_{eq}$ s at various temperatures.

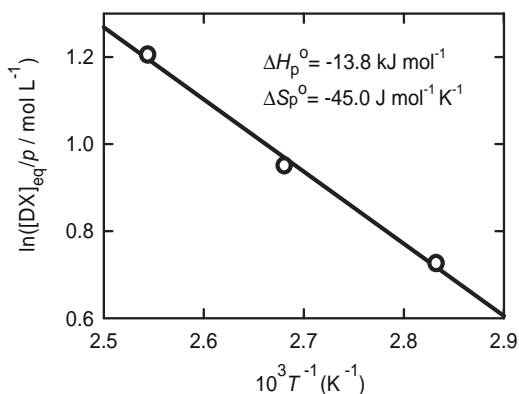


Figure 1.1 Plot of $\ln([DX]_{eq}/p)$ (where $p = (DP_n - 1)/DP_n$) on the reciprocal of the absolute temperature (Equation 1.8a). Bulk oligomerization of 1,4-dioxane-2-one (DX) initiated with the *n*-butyl alcohol/Sn(II) octoate mixture [28].

The slope and intercept of this dependence gives an access to ΔH_p° and ΔS_p° values, respectively [28]. Another typical method for determining ΔH_p° and ΔS_p° is based on the monomer and polymer combustion and specific heat measurements [29–36]. In turn, the thus-determined thermodynamic parameters allow an estimation to be made of the corresponding $[M]_{eq}$ values, this being especially useful when $[M]_{eq}$ is close to 0.

Values of thermodynamic parameters characterizing the polymerization ability of the most important cyclic and heterocyclic monomers are compared in Table 1.1. Equation 1.6 indicates that, at standard conditions, monomers for which $\Delta H_p^\circ < 0$ and $\Delta S_p^\circ > 0$ can be polymerized at any temperature, whereas those with $\Delta H_p^\circ > 0$ and $\Delta S_p^\circ < 0$ cannot be converted into linear macromolecules. In the most typical case—that is, when $\Delta H_p^\circ < 0$ and $\Delta S_p^\circ < 0$ —an increase in the polymerization temperature leads to an increase in $[M]_{eq}$ (Equation 1.7b). Eventually, at or above the so-called ceiling temperature (T_c ; Equation 1.9a), at which $[M]_{eq} = [M]_0$, formation of the high polymer does not occur. In contrast, for $\Delta H_p^\circ > 0$ and $\Delta S_p^\circ > 0$, $[M]_{eq}$ decreases with increasing temperature (Equation 1.7b) and there is another critical temperature—called the floor temperature (T_f , Equation 1.9b), at or below which polymerization is thermodynamically forbidden.

$$T_c = \frac{\Delta H_p^\circ}{\Delta S_p^\circ + R \ln [M]_0}; \quad (\Delta H_p^\circ < 0, \Delta S_p^\circ < 0) \quad (1.9a)$$

$$T_f = \frac{\Delta H_p^\circ}{\Delta S_p^\circ + R \ln [M]_0}; \quad (\Delta H_p^\circ > 0, \Delta S_p^\circ > 0) \quad (1.9b)$$

For example, tetrahydrofuran (THF) cannot be polymerized above $T_c = 84^\circ\text{C}$ [38], nor cyclo-octasulfur (S_8) below $T_f = 159^\circ\text{C}$ [16, 17]. However, for the majority of monomers listed in Table 1.1, T_c and T_f , for polymerization in the bulk, are well above or below the operable polymerization temperatures, respectively.

In general, the polymerization of cyclic monomers conforms to rules established for the hypothetical polymerization of cycloalkanes [15, 46]. The driving force for the polymerization of many cyclic compounds is their ring strain, which reflects the deviation from nondistorted bond angle values, bond stretching and/or compression, repulsion between eclipsed hydrogen atoms, and nonbonding interactions between substituents (angular, conformational and transannular strain, respectively). For systems in which the specific monomer–polymer–solvent interactions can be neglected, the enthalpy of polymerization may serve as a measure of the ring strain.

The polymerization of a majority of monomers is accompanied by an entropy decrease, due mostly to the loss in the translational degrees of freedom. In this situation, polymerization is thermodynamically allowed only when the enthalpic contribution into ΔG_p prevails (thus, when $\Delta H_p < 0$ and $\Delta S_p < 0$, the inequality $|\Delta H_p| > -T\Delta S_p$ is required; cf. Equation 1.4). Therefore, the higher the ring strain, the lower the resulting monomer concentration at equilibrium (Equation 1.7b).

Table 1.1 Standard thermodynamic parameters of polymerization of selected cyclic monomers.

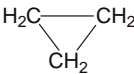
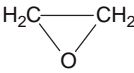
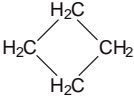
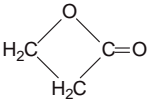
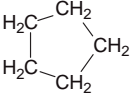
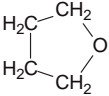
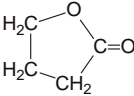
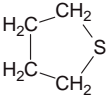
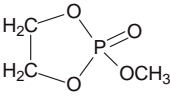
Monomer	Ring size	xy	$\frac{\Delta H_p^0}{\text{kJmol}^{-1}}$ ^a	$\frac{\Delta S_p^0}{\text{Jmol}^{-1}\text{K}^{-1}}$ ^a	$\frac{[\text{M}]_{\text{eq}}}{\text{molL}^{-1}}$ ^b	Reference(s)
 Cyclopropane	3	lc'	−113 ^c	−69.1 ^c	1.7×10^{-15}	[15]
 Ethylene oxide	3	gc	−140	−174	7.9×10^{-15}	[37]
 Cyclobutane	4	lc'	−105.1 ^c	−55.3 ^c	3×10^{-15}	[15]
 β-Propiolactone	4	lc'	−82.3	−74	3×10^{-11}	[29]
 Cyclopentane	5	lc'	−21.2 ^c	−42.7 ^c	3.4×10^{-1}	[15]
 Tetrahydrofuran	5	ls	−19.1 ^d	−74 ^d	3.3	[38]
 γ-Butyrolactone	5	lc	5.1	−29.9	3.3×10^3	[30]
 Tetrahydrothiophene	5	lc	−8 ^c	−85 ^c	1.2×10^3	[39]
 Ethylene phosphate	5	ss	−14.0	−13.5	1.62×10^{-2}	[40]

Table 1.1 Continued

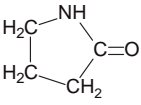
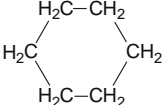
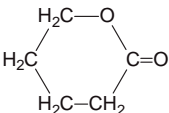
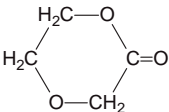
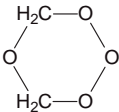
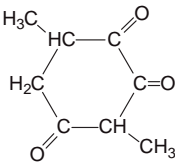
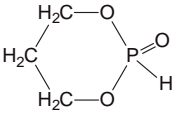
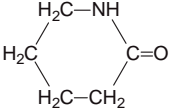
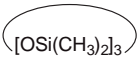
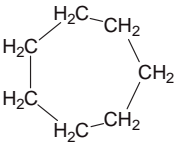
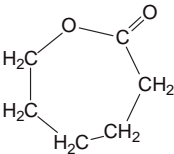
Monomer	Ring size	xy	$\frac{\Delta H_p^0}{\text{kJ mol}^{-1}}$ ^a	$\frac{\Delta S_p^0}{\text{J mol}^{-1} \text{K}^{-1}}$ ^a	$\frac{[\text{M}]_{\text{eq}}}{\text{mol L}^{-1}}$ ^b	Reference(s)
 γ-Butyrolactame	5	lc'	0.4	−30.1	5.1×10^2	[31]
 Cyclohexane	6	lc'	2.9 ^c	−10.5 ^c	1.36×10^2	[15]
 δ-Valerolactone	6	lc'	−27.4	−65.0	3.9×10^{-1}	[32]
 1,4-Dioxane-2-one	6	ls	−13.8 ^c	−45 ^c	2.5 ^f	[28]
 Trimethylene carbonate	6	ss	−26.4 ^g	−44.8 ^g	5.1×10^{-3}	[41]
 L,L-Lactide	6	ss	−22.9 ^h	−41.1 ^h	1.2×10^{-2}	[42]
 1,3-Propylene phosphite	6	ss ls	5.4 ⁱ −0.64 ^d	7.1 ⁱ −5.8 ^d	3.8 2.5	[43, 44]
 δ-Valerolactame	6	lc'	−7.1	−27.6	15.9	[31]

Table 1.1 Continued

Monomer	Ring size	xy	$\frac{\Delta H_p^0}{\text{kJ mol}^{-1}}$ ^a	$\frac{\Delta S_p^0}{\text{J mol}^{-1} \text{ K}^{-1}}$ ^a	$\frac{[M]_{\text{eq}}}{\text{mol L}^{-1}}$ ^b	Reference(s)
 Hexamethylcyclo- trisiloxane	6	ll	−23.4	−3.0	5.1×10^{-4}	[33]
 Cycloheptane	7	lc'	−21.8 ^c	−15.9 ^c	1.4×10^{-2}	[15, 46]
 ε-Caprolactone	7	lc'	−28.8	−53.9	5.1×10^{-2}	[34]
ε-Caprolactame	7	lc'	−13.8	4.6	2×10^{-2}	[31]
Cyclo-octasulfur	8	ls	13.2 ^j	19.4 ^j	40	[16, 17]
Octamethylcyclo- tetrasiloxane	8	ss	≈0	6.7 ^g	0.45	[45]
Tridecanolide	14	ll	−8	26	2.3×10^{-2k}	[35]
Pentadecanolide	16	ll	3	23	0.70 ^l	[36]

a At 298 K if not indicated otherwise.
b If not indicated otherwise calculated from Equation 1.7b, ΔH_p and ΔS_p^0 determined thermochemically; standard state: weight fraction = 1; concentrations recalculated from weight fractions to mol l^{−1}.
c ΔH_p and ΔS_p^0 estimated by semi-empirical calculations.
d ΔH_p and ΔS_p^0 determined from the experimental $[M]_{\text{eq}}$ versus T^{−1} dependence in monomer/polymer melt, using Equation 1.7a; standard state: 1 mol l^{−1}.
e ΔH_p and ΔS_p^0 determined from the experimental $[M]_{\text{eq}}$ versus T^{−1} dependence in monomer/polymer melt, using Equation 1.8a; standard state: 1 mol l^{−1}.
f At 373 K.
g ΔH_p and ΔS_p^0 determined from the experimental $[M]_{\text{eq}}$ versus T^{−1} dependence in THF solution, using Equation 1.7a; standard state: 1 mol l^{−1}.
h ΔH_p and ΔS_p^0 determined from the experimental $[M]_{\text{eq}}$ versus T^{−1} dependence in 1,4-dioxane solution, using Equation 1.7a; standard state: 1 mol l^{−1}.
i ΔH_p and ΔS_p^0 determined from the experimental $[M]_{\text{eq}}$ vs. T^{−1} dependence in CH₂Cl₂ solution, using Equation 1.7a; standard state: 1 mol l^{−1}.
j ΔH_p and ΔS_p^0 determined from the experimental $[M]_{\text{eq}}$ versus T^{−1} dependence in monomer/polymer melt, using Equation 1.7a; standard state: 1 mol kg^{−1}; concentration recalculated from mol kg^{−1} to mol l^{−1}.
k At 430 K.
l At 370 K.

The angle and bond deformations are most pronounced for the three- and four-membered rings, and this results in a high ring strain leading to negligible $[M]_{eq}$ values (Table 1.1). For example, the strain of a three-membered ring is so high that, although the formation of three-membered α -lactone intermediates was postulated on the basis of quantum mechanical calculations [47], the cyclic ester has never been isolated.

The five- and six-membered cycles are the least strained, and some of these are ultimately unable to undergo polymerization. The ring strain for these monomers is derived mostly from the gauche interactions between C–H bonds in the neighboring CH_2 groups, or between C–H bonds and the lone electron pairs at the endocyclic oxygen atom. Eventually, cyclopentane and THF show only moderate enthalpies of polymerization that lead to the relatively high $[M]_{eq}$ s. However, the introduction of a sulfur atom or a carbonyl group into the five-membered ring makes the resultant compounds incapable of high polymer formation under normal conditions. This is caused either by an increase in the atomic radius of the S heteroatom, or by a decrease in the number of bond oppositions, due to sp^2 hybridization of the carbon atom in the $>C=O$ group. The six-membered alkanes and ethers assume the most convenient chair conformation in which the energy of the conformational interactions is negligible and the hypothetical $[M]_{eq}$ is well above any possible $[M]_0$ values. In contrast, the presence of ester or siloxane moieties in the six-membered ring increases the strain in such a way that δ -valerolactone, DX, lactides (LA), cyclic carbonates and hexamethylcyclotrisiloxane (D_3) can be readily polymerized. The carbonyl group introduces a certain measure of strain into six-membered rings due to the flat geometry of the ester moiety ($-CH_2-C(=O)-O-$). Also, in the almost flat D_3 molecule the $-Si-O-Si-$ and $-O-Si-O-$ bond angle distortions provide considerable polymerization enthalpy.

The thermodynamic data in Table 1.1, characterizing larger cyclic monomers, suggest that an increase in ring size leads to rather small ring strain (if any) and in turn to an increase in the polymerization entropy. The latter effect is due to a relatively high flexibility of the long polymethylene, polysulfur and polysiloxane sequences in the resultant polymer chain. Thus, for this group of monomers polymerization becomes entropy-driven. However, as mentioned earlier, the formation of a high polymer from cyclo-octasulfur is possible only above $T_f = 159^\circ C$, whereas the polymerization of octamethylcyclotetrasiloxane and macrolides can proceed both at ambient and elevated temperatures.

Figure 1.2 illustrates the characteristic changes in standard thermodynamic parameters with increasing size of cyclic monomer, as shown by the example of lactones bulk polymerization. Similar dependencies were also observed for other monomers, though with only slight changes in the position of the local minima or maxima on the thermodynamic parameter–ring size dependencies [21, 22, 26].

Similar rules are also valid for the ring-opening metathesis polymerization (ROMP) of cyclic olefins [10, 13, 48, 49]. We refrain here from more providing a detailed analysis of this group of monomers; rather, it is sufficient to repeat an opinion expressed recently by Grubbs that “... the most favorable conditions for a

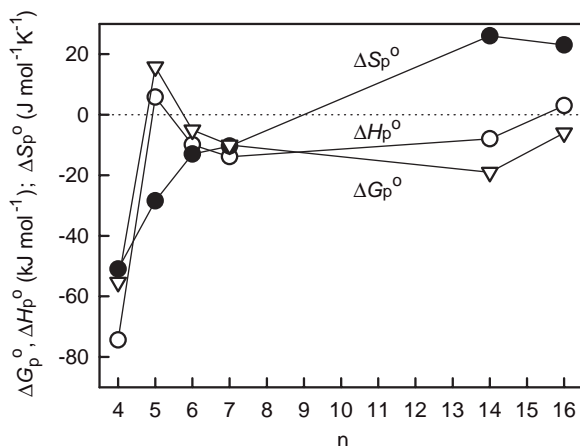


Figure 1.2 The dependencies of standard Gibbs energy (ΔG_p° ; ∇), enthalpy (ΔH_p° ; \circ) and entropy (ΔS_p° ; \bullet) of lactones polymerization on their ring sizes (n). The temperature was dependent on the lactone, and ranged from 350 to 430 K, monomer and polymer liquid. Data taken from Refs [29, 30, 32, 34–36].

successful ROMP reaction is to use the highest monomer concentration at the lowest temperature possible” [13].

It is also worth remembering that, in contrast to the cyclic monomers, the large majority of unsaturated compounds polymerize, leaving a relatively low monomer concentration at the point of equilibrium. Indeed, when considering the nonsolvent, bulk polymerization of monomers such as ethylene, methyl acrylate or styrene, then at 25 °C the situation is that $[M]_{eq} \approx 10^{-10}$, 10^{-9} or 10^{-6} mol l⁻¹, respectively. When unsaturated monomers providing steric hindrance in the polymer units are considered, then homopolymerization may be hampered; here, 1,1-diphenylethylene is the best example, as the joining of two consecutive units is prohibited. The introduction of a second (even small) substituent causes a considerable increase in $[M]_{eq}$. For example, in the case of methyl methacrylate or α -methylstyrene, $[M]_{eq} = 10^{-3}$ or 2.2 mol l⁻¹ at 25 °C, respectively, have been determined [50, 51].

Finally, it must be stressed that the analysis of a given polymerization process, based on values of the corresponding thermodynamic parameters available in the literature, should be approached with some degree of caution. First, ΔH_p° and ΔS_p° depend substantially on the monomer and polymer states. For example, thermochemical measurements gave for 16-membered pentadecanolactone in the liquid phase $\Delta H_p^\circ = 3$ kJ mol⁻¹ and $\Delta S_p^\circ = 23$ J mol⁻¹ K⁻¹, whereas in the crystalline phase $\Delta H_p^\circ = -39$ kJ mol⁻¹ and $\Delta S_p^\circ = -86$ J mol⁻¹ K⁻¹ [36]. The difference between these sets of parameters is caused by corresponding phase transitions (crystallization/melting) enthalpies and entropies, although for the melt or solution polymerization analysis the liquid-phase parameters are most likely correct. ΔS_p° determined

at different standard states (e.g. 1 mol l^{-1} and weight fraction = 1) cannot be compared directly, and so must be recalculated. For example:

$$\Delta S_p^\circ(\text{mol l}^{-1}) = \Delta S_p^\circ(\text{wt. fraction}) + R \ln \frac{x/\text{wt. fraction}}{1/\text{mol l}^{-1}} \quad (1.10)$$

where x denotes a weight fraction corresponding to 1 mol l^{-1} for a given monomer.

Moreover, Equation 1.9 show that the values of critical temperatures depend directly on the starting monomer concentration. Fortunately, the values for bulk monomer or for 1 mol l^{-1} are almost exclusively reported.

1.2.2

Selected Particular Cases

The discussion of the thermodynamic prerequisites necessary for predicting given monomer polymerizability, as presented in Section 1.2.1, was based on the following assumptions:

- Polymerization is carried out in the homogeneous medium (e.g. monomer/polymer melt or monomer/polymer/solvent solution).
- Monomer–polymer–solvent interactions can be neglected.
- A high molar mass polymer is exclusively formed.

Deviations from these assumptions lead, in certain polymerization systems, to interesting phenomena, an instructive example of which is provided by the solid-state 1,3,5-trioxane polymerization reviewed extensively in Ref. [3b], Section 7.3. Some other pertinent examples are briefly discussed below.

1.2.2.1 Polymerization in Heterogeneous Systems

The polymerization of industrially important monomers, such as DX or LA, is usually carried out above the melting temperature of their polymers in an homogeneous melt. Under these conditions [i.e. $>110^\circ\text{C}$ for poly(DX) and 180°C for poly(LA)], the equilibrium monomer concentrations are relatively high—namely, $[\text{DX}]_{\text{eq}} > 2.5 \text{ mol l}^{-1}$ and $[\text{LA}]_{\text{eq}} > 0.32 \text{ mol l}^{-1}$, due to the moderate ring strain of the six-membered monomers. However, the molar fraction of the unreacted monomers can be reduced by aging the living polymerization mixtures below the melting temperature of the polyesters formed. Under these modified conditions, poly(DX) or poly(LA) crystallize, while the volume of the liquid phase (in which the unreacted monomer remains) decreases simultaneously. Subsequently, $[\text{M}]$ increases temporarily above $[\text{M}]_{\text{eq}}$, after which an additional polymerization of the monomer proceeds, leading to an apparent decrease in $[\text{M}]_{\text{eq}}$ (actually the molar fraction of M). The eventual result is an almost complete consumption of the monomer. This result is achieved despite the conclusions that may be drawn from the values of thermodynamic parameters provided in Table 1.1 for both of the monomers under discussion [52, 53].

1.2.2.2 Monomer–Polymer–Solvent Interactions

For some cyclic monomers, such as six-membered propylene phosphite (PP) exerting a small ring strain, the energy of interaction between the monomer, polymer and solvent appears to be comparable with the ring strain energy. It has been shown that, for PP, ΔH_p° and ΔS_p° can change their signs when the conditions of polymerization are changed from polymerization in a monomer/polymer melt to that in methylene chloride, and vice versa (Table 1.1) [43, 44].

Ivin and Leonard, starting from Flory–Huggins theory [54], derived an equation relating the volume fractions of monomer, polymer and solvent (Φ_m , Φ_p and Φ_s), the monomer–solvent, polymer–solvent and monomer–polymer interaction parameters (χ_{ms} , χ_{ps} and χ_{mp}) with the absolute (i.e. independent of the polymerization conditions) thermodynamic parameters [55]:

$$\Delta H_p^\circ/RT - \Delta S_p^\circ/R = \ln \Phi_m + 1 + \left(\chi_{ms} - \chi_{ps} \left(\frac{V_m}{V_s} \right) \right) \Phi_s + \chi_{mp} (\Phi_p - \Phi_m) \quad (1.11)$$

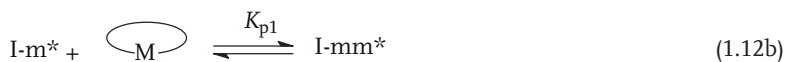
where V_m and V_s denote the molar volumes of monomer and solvent.

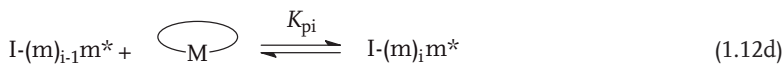
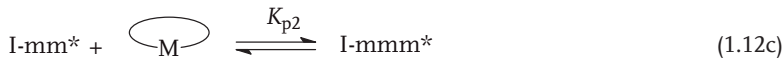
Equation 1.11 applied for correlation of the experimental data: $[PP]_{eq}$ –temperature (for both bulk and solvent process) allowed, eventually, an estimation to be made of the absolute thermodynamic parameters of polymerization: $\Delta H_p^\circ = -0.64 \text{ kJ mol}^{-1}$ and $\Delta S_p^\circ = -5.8 \text{ J mol}^{-1} \text{ K}^{-1}$ (cf. the apparent parameters in Table 1.1) [44].

The specific monomer–solvent interaction plays also an important role in the cationic ROP of THF, as it exerts a considerable influence on the dependency of $[THF]_{eq}$ on $[THF]_0$ [56]. The observed phenomenon was explained by taking into account the higher nucleophilicity of THF monomer than that of the poly(THF) repeating units. Consequently, it was assumed that the stronger interaction between THF and solvent was only partially compensated by the comparatively weaker solvent–poly(THF) interactions. For a given $[THF]_0$, $[THF]_{eq}$ was seen to increase in the following order: $\text{CCl}_4 < \text{C}_6\text{H}_6 < \text{CH}_2\text{Cl}_2 < \text{CH}_3\text{NO}_2$ —that is, in the direction of the strongest monomer–solvent interactions. For instance, $[THF]_{eq}$ equal to 4.0, 4.3, 5.6 and 6.0 mol l^{-1} , respectively, were determined for $[THF]_0 = 6 \text{ mol l}^{-1}$ at 25°C [56]. As might be expected, both ΔH_p° and ΔS_p° were increased slightly in this order.

1.2.2.3 Thermodynamics of Oligomerization

It is well known that, for shorter chains (approximately up to $DP_n = 20$), the position of the cyclic monomer–linear chain depends on its degree of polymerization:





The equilibrium constants for the first few monomer additions are not the same, as for an addition to a high polymer ($K_{p0} \neq K_{p1} \neq K_{p2} \neq \dots K_{pi}$) due to an influence of the head- and tail-end-groups and usually K_{p0} , K_{p1} , K_{p2} ,... are larger than K_{pi} . Thus, the Gibbs energy for the oligomerization process must be expressed as shown in Equation 1.5. Moreover, a higher equilibrium monomer concentration for the higher number average degree of oligomerization should be expected, as the corresponding equilibrium constants become smaller for longer chains:

$$[\text{M}]_{\text{eq}} = \frac{[\text{I-(m)}_i\text{m}^*]}{K_i [\text{I-(m)}_{i+1}\text{m}^*]} \quad (1.13)$$

Indeed, Heitz *et al.* studied the cationic oligomerization of THF in CH_2Cl_2 as solvent at 10°C , using acetic anhydride as the transfer agent, and observed a gradual increase in $[\text{THF}]_{\text{eq}}$ from 1 to 4.3 mol l^{-1} for DP_n of poly(THF) increasing from 1 to 15 [57]. For $DP_n \geq 15$, the discussed dependence reached a plateau; thus, $[\text{THF}]_{\text{eq}} = 4.3 \text{ mol l}^{-1}$ was seen to be characteristic for the high polymer formation under the applied polymerization conditions ($[\text{THF}]_0 = 6 \text{ mol l}^{-1}$, CH_2Cl_2 solvent, 10°C). A rigorous treatment of the equilibrium oligomerization, leading alternatively to Equation 1.8a, and allowing determination of the standard thermodynamic parameters from the experimental $\ln[\text{M}]_{\text{eq}}$ versus T^{-1} dependence, is provided in Ref. [57].

More recently, the oligomerization of DX monomer in 1,4-dioxane as solvent and coinitiated with butyl alcohol (BuOH), was studied using a variety of starting monomer concentrations at approximately constant $[\text{DX}]_0/[\text{BuOH}]_0$ ratios [28]. The resultant $[\text{DX}]_{\text{eq}}$ versus $[\text{DX}]_0$ dependencies are shown in Figure 1.3.

Independent of temperature (80, 100 or 120°C), $[\text{DX}]_{\text{eq}}$ was seen to increase with increasing $[\text{DX}]_0$ up to $[\text{DX}]_0 \approx 4 \text{ mol l}^{-1}$, and then to level off at a constant value, independent of $[\text{DX}]_0$. Again, the observed behavior could be explained by assuming an increase of DP_n of the linear oligo(DX), this being in equilibrium with the DX monomer, for a higher $[\text{DX}]_0$.

From the theory of polymerization thermodynamics, it can be deduced that in the vicinity of the ceiling (T_c) and at higher temperatures, or in the vicinity of the floor (T_f) and at lower temperatures, no high molar mass polymer can be formed. Yet, the analysis provided above suggests that formation of shorter, oligomeric chains may be possible under these conditions. For example, γ -butyrolactone (BL) has a hypothetical equilibrium monomer concentration at 25°C which is equal to $3.3 \times 10^3 \text{ mol l}^{-1}$, which exceeds 250-fold the BL concentration in bulk (Table 1.1); the hypothetical T_c is below 0 K (!), because $\Delta H_p^\circ > 0$ and $\Delta S_p^\circ < 0$ (Equation 1.9a)

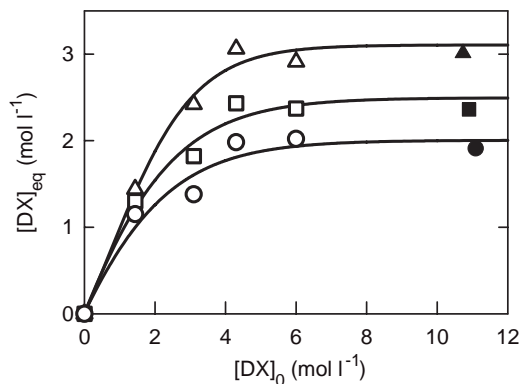
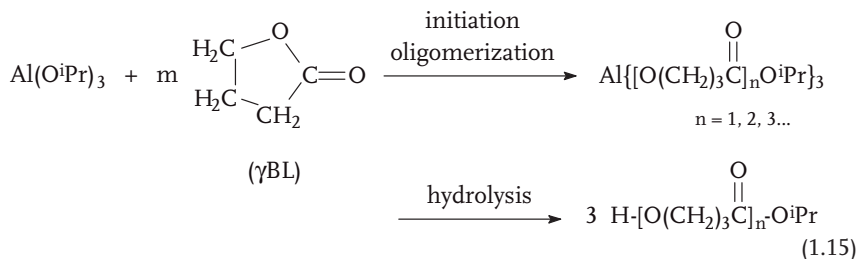


Figure 1.3 Plots of equilibrium monomer concentrations ($[DX]_{eq}$) on monomer concentration in the feed ($[DX]_0$) as obtained in a DX/tin octoate ($Sn(Oct)_2$)/BuOH polymerization system. Conditions: $[Sn(Oct)_2]_0 = 10^{-2} \text{ mol l}^{-1}$. Open symbols indicate polymerization in 1,4-dioxane solvent; solid symbols indicate bulk polymerization. Temperatures (in $^{\circ}\text{C}$): 80 (\circ , \bullet), 100 (\square , \blacksquare) and 120 (\triangle , \blacktriangle).

for this monomer. Consequently, BL is typically considered to be a monomer that is incapable of polymerizing [58], although it does not mean that BL cannot undergo ring-opening reactions at all. For most short chains the inequality takes place: $[BL][poly(BL)_i] \gg [poly(BL)_{i+1}]$, and the ‘entropic term’ may outweigh the $\Delta H_i^{\circ} \geq 0$, making $\Delta G_i < 0$ (Equation 1.14); hence, shorter chains are allowed to be formed.

$$\Delta G_i = \Delta H_i^{\circ} - T\Delta S_i^{\circ} - RT \ln \frac{[BL][poly(BL)_i]}{[poly(BL)_{i+1}]} \quad (1.14)$$

Indeed, some time ago it was reported that the ROP (actually oligomerization) of BL initiated with $\{Al(O^iPr)_3\}_3$ readily provided a series of poly(BL) chains:



Mass spectrometric measurements revealed the formation of $iPrO-(bl)_n-H$ oligomers with DP up to 10 [59–61].

In addition, poly(BL) of moderate molar mass (M_n up to 3.5×10^3) was prepared at high pressure (2×10^4 bar) [62] in agreement with the T_c –pressure relationship as predicted by the Clausius–Clapeyron equation:

$$\ln T_c(p) = \ln T_c(p = 1 \text{ bar}) + \frac{V_p - V_m}{\Delta H_p^o} p \quad (1.16)$$

The term $V_p - V_m$ is typically negative since, in the majority of polymerizations, a molar volume contraction occurs of the reacting mixture. Under high pressure, liquid BL is transformed into crystalline poly(BL); in this case $\Delta H_p^o = -6.8 \text{ kJ mol}^{-1}$ has been determined [30]. Thus, T_c increases considerably under the high pressures that eventually allow poly(BL) to be prepared.

It is also worth noting that the ability to oligomerize, of the otherwise nonhomopolymerizable monomers, creates a possibility of copolymerization above or below their T_c or T_b , respectively. These instructive examples are derived from the coordination copolymerization of BL with ϵ -caprolactone (CL) [59, 63, 64] and the anionic copolymerization of S_8 with three-membered alkylene sulfides (thiiranes) [65, 66], both of which produce high-molar mass copolymers (for further details, see Section 1.2.4).

1.2.3

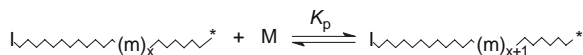
Thermodynamics of Macrocyclization

In ROP, the polymer repeating units usually contain the same reactive groups as those present in monomer, and which are responsible for propagation. Consequently, apart from propagation, a variety of reactions of chain transfer to the macromolecule with chain rupture can take place (Scheme 1.1). These side reactions—either unimolecular and/or bimolecular—lead unavoidably to the formation of macrocyclic molecules and/or to the segmental exchange (scrambling) of macromolecules. The consequence of the latter reaction is merely a broadening of the molar mass distribution of the polymer formed. Macrocyclization and segmental exchange reactions have been observed in the polymerization of various cyclic monomers, including alkenes [67], ethers [68], acetals [69], esters [70], amides [71], siloxanes [72] and sulfides [73]. Because of the potentially serious consequences of the macrocyclization limiting possibility of the controlled polymer synthesis, the thermodynamics of this process has undergone extensive study and review in the past (e.g. see Refs [3b, 22, 26, 74]).

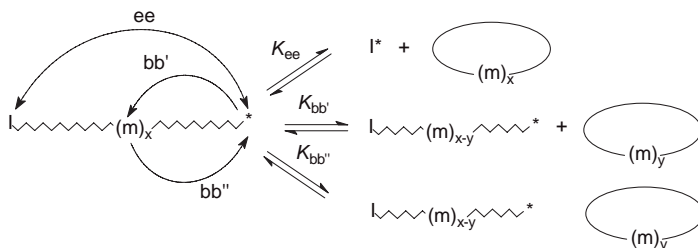
Cyclic oligomers can be formed in two types of reaction: end-to-end closure and back-biting. The latter reaction proceeds via either a nucleophilic attack of the active species on its own macromolecular chain (anionic and coordination processes), or by a nucleophilic attack of the repeat unit (cationic process) on the active species in the same macromolecule (Scheme 1.1).

In the case of back-biting and a high molar mass of the linear polymer fraction, the expression for the corresponding equilibrium constant reads:

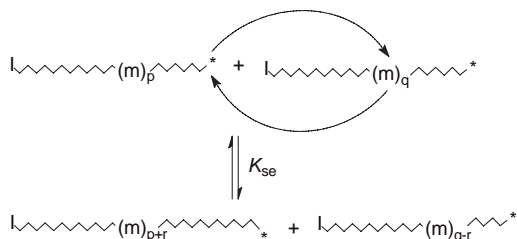
(a) Propagation



(b) Macrocyclization



(c) Segmental exchange



K_p = equilibrium constant of propagation; K_{ee} = equilibrium constant of end-to-end cyclization
 $K_{bb'}$, $K_{bb''}$ = equilibrium constants of back-biting; K_{se} = equilibrium constant of segmental exchange

Scheme 1.1 General scheme of ring-opening polymerization accompanied by chain transfer to macromolecule with chain rupture.

$$K_{bb}(y) = \frac{[\dots -\text{m}_x - \dots][\text{M}(y)]_{\text{eq}}}{[\dots -\text{m}_{x-y} - \dots]} \approx [\text{M}(y)]_{\text{eq}} \quad (1.17)$$

where $\text{M}(y)$ represents the macrocycle containing y repeating units of $\dots -\text{m} - \dots$

Theoretical considerations based on the Jacobson–Stockmayer theory [75, 76] led to the conclusion that, for nonstrained cycles in θ solvent:

$$[\text{M}(y)]_{\text{eq}} \sim y^{-5/2} \quad (1.18)$$

Thus, the equilibrium concentration of a given macrocycle should decrease monotonically with increasing ring size. Detailed studies of the equilibrium distribution of cyclic siloxane oligomers provided a very good agreement between the theoretical and experimental values for $y > 25$; that is, for this range of cyclopoly-siloxane sizes the plot of $\ln[\text{M}(y)]_{\text{eq}}$ versus $\ln y$ was a straight line with a slope of $-5/2$ [76]. Some deviation from the theoretical slope observed for $y > 40$ was

ascribed to the excluded volume effect [77, 78]. Careful studies of the anionic polymerization of CL revealed that, in the macrocycle sizes from $\gamma = 3$ to 7, the slope of $\ln [M(\gamma)]_{\text{eq}}$ versus $\ln \gamma$ dependence was slightly lower than the theoretical counterpart, and equaled -2.2 [79]. Such deviation has been attributed to a screening of the given ester group from the active center by other atoms of its own cyclic molecule (i.e. to conformational hindrance).

In agreement with expectation, the concentration of nonstrained cycles—in line with Jacobson–Stockmayer theory—should be temperature-independent. The results of measurements performed by Ito and Yamashita [80] have shown that the concentration of cyclic CL oligomers changed very little in the temperature range from -78 to 50°C . This observation led to the conclusion that $\Delta H_p(i) \approx 0$ (where $i \geq 2$). Likewise, for other polymerizing systems in which ring-chain equilibria take place, it is generally accepted that the propagation (or depropagation) of larger cyclics is accompanied by enthalpy changes that are equal to zero [76].

One important factor from a practical point of view is the critical concentration of the macrocycles (i.e. $\Sigma \gamma [M(\gamma)]_{\text{eq}}$), the parameter which indicates the concentration of monomer which eventually will be converted into the macrocyclic fraction. For example, in CL and DX anionic and/or coordination polymerization, $\Sigma \gamma [M(\gamma)]_{\text{eq}}$ has been determined as being equal to 0.25 mol l^{-1} (25°C , THF) [79–81] and 0.95 mol l^{-1} (bulk, 100°C) [28], respectively. Figure 1.4 shows a typical size-exclusion chromatography (SEC) trace revealing the presence of a series of cyclic CL oligomers in the living, equilibrated polymerization mixture.

Cyclic oligomers are usually considered to be a contamination of the high polymers, as their presence results in a deterioration of the mechanical properties of

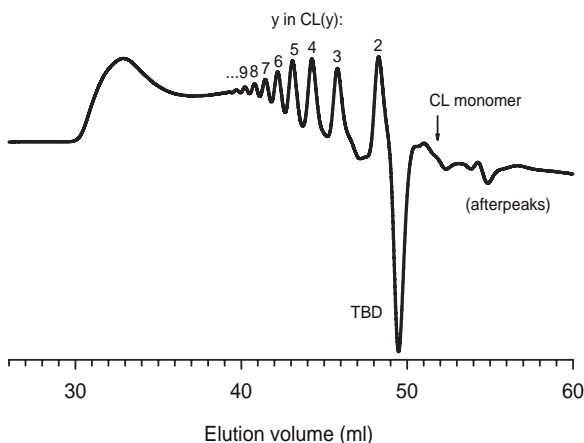


Figure 1.4 Size-exclusion chromatography of a living, equilibrated polymerization mixture: ϵ -caprolactone (CL)/ triazabicyclodecene (TBD)/benzyl alcohol (BzOH). Conditions: $[CL]_0 = 0.5 \text{ mol l}^{-1}$, $[TBD]_0 = 2 \times 10^{-2} \text{ mol l}^{-1}$, $[BzOH]_0 = 2.5 \times 10^{-3} \text{ mol l}^{-1}$; THF solvent, 80°C (A. Duda and A. Kowalski, unpublished results).

the final product. The formation of a cyclic fraction is especially undesirable when the synthesis of a functional polymer (e.g. oligodiols) is attempted, because cyclic macromolecules do not contain functional groups and cannot participate in chain extension reactions. Hence, it is interesting to note in this context, that two different phenomena can take place in ROP, namely kinetic enhancement in cyclics and kinetic enhancement in linear macromolecules. Thus, before the thermodynamic equilibrium in cyclics is reached—that is, during the kinetically controlled period—the concentration of either the cyclics or linear macromolecules may exceed those at thermodynamic equilibrium. The polymerization of ethylene oxide (EO) provides an instructive example. Here, the anionic process is practically devoid of macrocyclics formation, whereas the cationic process proceeds with significant amounts of cyclic oligomers that are formed in addition to the linear polymer. Thus, the final content of the cyclic dimer (1,4-dioxane) may be as high as 90% [82]. The phenomena of kinetic depression or even elimination of the cyclic oligomers fraction are described in more detail in Section 1.3.2.3.

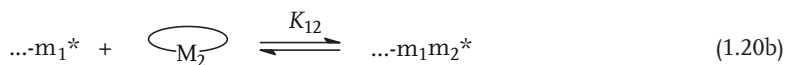
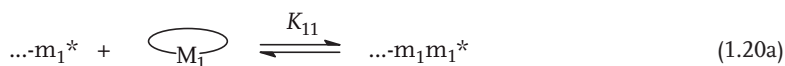
1.2.4

Equilibrium Copolymerization

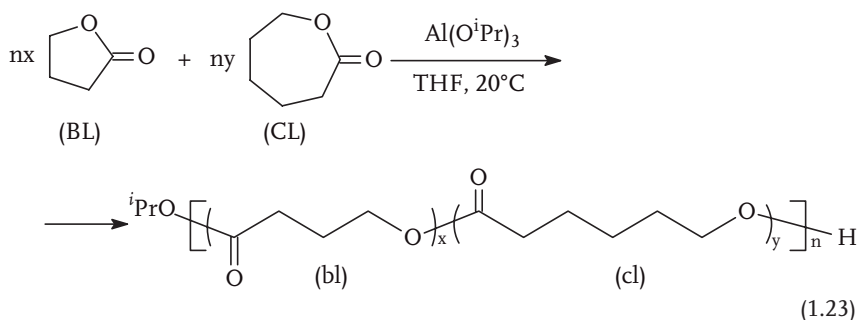
The stoichiometric equation for copolymerization includes two or a higher number of comonomers:



Similarly, as for homopolymerization, the difference in free enthalpy of the copolymer and comonomers (ΔG_{co}) can be used as a formal criterion of a copolymerizability in the given comonomers system: that is, copolymerization is possible only when $\Delta G_{co} < 0$. It must be stressed, however, that for copolymerization $\Delta G_{co} = 0$ is a necessary (but not sufficient) condition in order for the thermodynamic equilibrium to take place. This is due to the higher degrees of freedom in the case of the copolymerization. Even when the partial equilibrium described by Equation 1.19 is established, the system can—in principle—spontaneously undergo an infinite number of reactions that lead to copolymers of different composition and/or microstructure [83]. In practice, the simplified, diad model of copolymerization is assumed; this consists of four reversible reactions where the structure of the repeating unit preceding the active center has no influence on the corresponding homo- and cross-propagation equilibria constants (Equation 1.20).



The results of more recent studies have revealed that copolymerization of the nonhomopolymerizable BL with CL and other monomers provides high molar mass polymers [59, 63, 64]. For example:



The dependence of γ -butyryl repeating unit (bl) content in the copolymer (F_{bl}), on the BL monomer content in the feed (f_{BL}) is shown in Figure 1.5. As might be expected from the copolymerization of a monomer which is unable to provide high polymers, even with a major excess of BL in the feed ($[\text{BL}]_0/[\text{CL}]_0$ equal to 11.9), the -bl- content in the copolymer should not exceed 50 mol%. Thus, one could expect the formation of a close to alternating copolymer at a sufficiently large excess of BL. In fact, the ^{13}C NMR spectral analysis pointed towards a pseudoperiodic copolymer structure [59]. The BL/CL copolymer synthesis was successful, despite the fact that BL monomer addition to its own -bl* active chain ends was highly reversible, as the -bl* unit could be blocked via a practically irreversible CL addition. In addition, when BL is present in high excess over CL (i.e. $[\text{BL}] > [\text{CL}]$), then BL addition proceeds faster than that of CL.

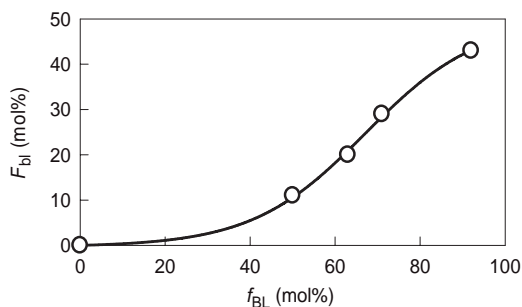


Figure 1.5 Dependence of γ -butyryl (bl) units content in the γ -butyrolactone (BL)/ ϵ -caprolactone (CL) copolymer ($F_{\text{bl}} = 100[\text{bl}]/([\text{bl}] + [\text{cl}])$), on the BL monomer content in the feed ($f_{\text{BL}} = 100[\text{BL}]_0/([\text{BL}]_0 + [\text{CL}]_0)$). cl = ϵ -caproyl unit content [89].

Similarly, the earlier studies of S_8 copolymerization with thiiranes (e.g. propylene sulfide; PS), at temperatures below T_f for S_8 homopolymerization, revealed that the average sulfur rank in the copolymer (i.e. average x in $-\text{[CH}_2\text{CH(CH}_3\text{)S}_x\text{]}_n-$) was increased from 1 to 7 when the $8[S_8]_0/[PS]_0$ ratio was increasing from 0 to 10 [65, 66].

The situation of a monomer incapable of producing high polymers above T_c or below T_f is similar to a that of monomer which cannot homopolymerize at a given temperature but is reaching its polymer–monomer equilibrium. Under these conditions, no further increase in monomer consumption takes place; however, the introduction at this moment of another monomer—which is able to homopolymerize—leads to the formation of a block copolymer with a bridge that follows the first homopolymer block and the build of the gradient copolymer. This was observed when LA was first brought to the polymer–monomer equilibrium, after which CL was introduced into the system [90].

1.2.5

Molar Mass Distribution in the Equilibrium Polymerization

The living polymerization of strained three- and four-membered monomers typically provides polymers with a narrow molar mass distribution, best described by the Poisson function [91], for which the dispersity indexes ($D = DP_w/DP_n = M_w/M_n$) assume values in the range $\sim 1.25 \geq D > 1$, depending on the polymer chain length (Equation 1.24). As discussed earlier, the polymerization of these monomers is essentially irreversible.

$$D = \frac{DP_w}{DP_n} = \frac{DP_n}{(1 + DP_n)^2} \quad (1.24)$$

For the larger ring sizes, both propagation and depropagation must be taken into account (Equation 1.3b), and a certain measurable concentration of the unreacted monomer appears when the system comes to thermodynamic equilibrium ($[M]_{eq} = 1/K_p = k_d/k_p$). In this case, the molar mass distribution may be described by the most probable (Flory–Schultz) distribution function [92], for which:

$$D = \frac{DP_w}{DP_n} = 2 - \frac{1}{DP_n} \quad (1.25)$$

Consequently, for the high molar mass polymer, $D = 2$ should be expected, whereas even for monomers such as lactides having a relatively high $[LA]_{eq}$ at typical polymerization temperatures (0.055 mol l^{-1} at 80°C [42]), values of $D < 1.15$ are often reported (see Ref. [93] and references cited therein).

The reason for such a situation occurring is related to the fact that the equilibria at which the polymerizations are stopped are in fact incomplete. Examples of numerically computed dependences of DP_w/DP_n on monomer conversion,

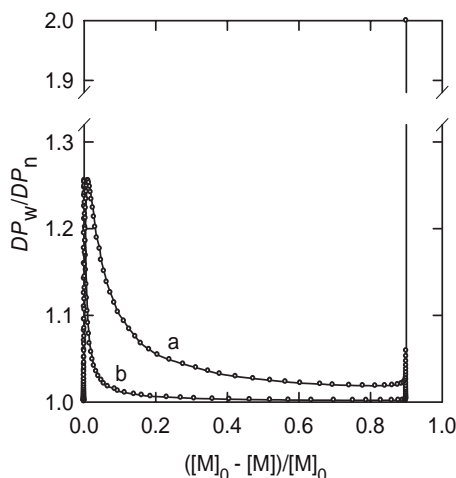


Figure 1.6 Computed dependence of dispersity index (DP_w/DP_n) of the polymer formed by living polymerization with reversible propagation in relation to the degree of monomer conversion ($([M]_0 - [M]_{eq})/[M]_0$). Assumptions: $[M]_0 = 1.0 \text{ mol l}^{-1}$; $[I]_0 = 10^{-2}$ (curve a), 0.10^{-3} (curve b) mol l^{-1} ; $[M]_{eq} = 0.1 \text{ mol l}^{-1}$ [94].

resulting from depropagation, are shown in Figure 1.6 [94]. These reversible polymerizations can be living and, despite the remarkably high $[M]_{eq}$, a polymer with a D -value close to that resulting from a Poisson distribution can be obtained under kinetically controlled conditions, and even at high yield close to ‘complete’ monomer conversion. At this point it is worth noting that, to reach $D = 1.99$ —which is characteristic of an almost-complete equilibrium—it would take almost 100-fold longer than would be necessary for a 99.9% monomer conversion (i.e. 0.999 $([M]_0 - [M]_{eq})/[M]_0$), under the assumed polymerization conditions [94].

Chain-transfer side reactions (see Scheme 1.1) can also cause substantial increases in D -values. Macrocyclization is particularly poor in this respect, leading to a complete equilibrium and an especially broad molar mass distribution (see e.g. Figure 1.4). On the other hand, a reversible polymerization devoid of macrocyclization, but accompanied by the segmental exchange reactions, can fulfill the criteria of the living process [95–99]. However, in this case the D -value also increases with conversion, reaching at equilibrium a value which is predicted by Equation 1.24 and characteristic of the most probable molar mass distribution. Figure 1.7 illustrates the dependence of M_w/M_n determined for LA polymerization initiated with Sn(II) alkoxide [98].

It is remarkable that a M_w/M_n ratio of approximately 80% for LA conversion does not differ much from that expected for a Poisson distribution. Finally, the same system, when nearing the thermodynamically controlled region, the M_w/M_n is approaching ≈ 2 .

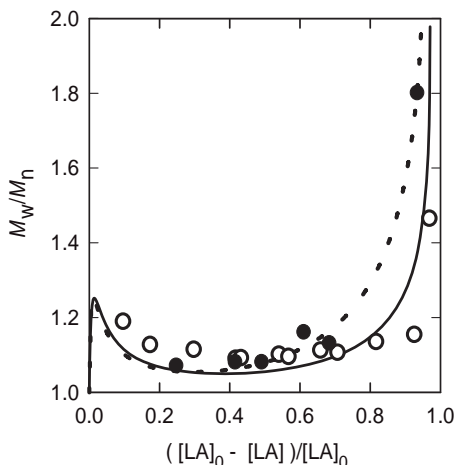


Figure 1.7 Dependence of dispersity indexes (M_w/M_n) of poly(L-lactide) on the degree of monomer conversion. Conditions of polymerization: $[LA]_0 = 1.0 \text{ mol l}^{-1}$, THF solvent; $[Sn(OBu)_2]_0$ (in mol l^{-1}) = 5×10^{-3} (●), 8.9×10^{-3} (○); temperatures: 80°C (●), 20°C

(○). The points represent experimental data; the lines were computed from the kinetic scheme in which reversible propagation is accompanied by the segmental exchange reactions [Scheme 1.1, reactions (a) and (c)] [98].

1.3

Kinetics of Ring-Opening Polymerization

1.3.1

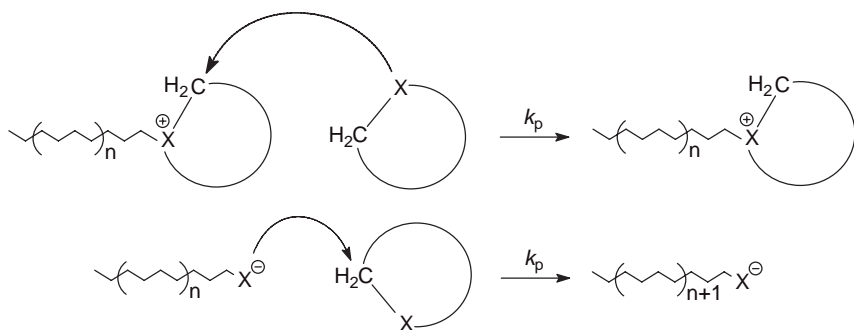
Thermodynamic and Kinetic Polymerizability

Polymerizability, in terms of the kinetics of propagation formalism, is related to a sign of the molar free enthalpy (Gibbs energy) of activation (ΔG_p^\ddagger), this being a measure of the energy barrier in the elementary act of propagation (Equations 1.2 or 1.3b), for which ΔG_p^\ddagger assumes exclusively positive values. For example, when $\Delta G_p^\ddagger < 0$ this means that a given reaction is more complex and does not exclusively correspond to the elementary act of macromolecular chain growth. The resultant rate constant of propagation (k_p ; see Equation 1.26 [100]) for a given mechanism and structure of active centers should assume values assuring operable polymerization times at a given temperature.

$$k_p = \frac{k_b T}{h} \exp\left(-\frac{\Delta G_p^\ddagger}{RT}\right) = \frac{k_b T}{h} \exp\left(-\frac{\Delta H_p^\ddagger}{RT} + \frac{\Delta S_p^\ddagger}{R}\right) \quad (1.26)$$

where k_b , h , ΔH_p^\ddagger , ΔS_p^\ddagger denote the Boltzman constant, Planck constant, enthalpy and entropy of activation, respectively.

As highlighted in Section 1.1, the fulfillment of thermodynamic requirements is a necessary—but not sufficient—prerequisite for a polymerization to occur. A typical example is the polymerization of THF; here, although there is no anionic



Scheme 1.2 Comparison of cationic and anionic propagation pathways in the ROP of heterocyclic monomers.

pathway, a cationic process provides poly(THF) readily, at least at temperatures below T_c [3]. In the cationic polymerization, ring opening proceeds with methylene carbon–heteroatom bond ($-\text{CH}_2-\text{X}-$) cleavage in the ‘activated’ monomer as a fragment of the active center (onium ion), whilst the anionic propagation requires $-\text{CH}_2-\text{X}-$ bond splitting in the monomer *per se* (Scheme 1.2).

Thus, for the ‘bare’ monomer the high ΔG_p^\ddagger (or actually ΔH_p^\ddagger due to the high $-\text{CH}_2-\text{O}-$ bond strength), and therefore low k_p , preclude anionic propagation. In contrast, for the much more strained EO monomer, both anionic and cationic ring opening will function equally well.

In general, ‘thermodynamic polymerizability’ cannot be taken as a direct measure of a monomer’s reactivity. For example, the rate constants for the basic hydrolysis of BL and CL (under comparable conditions) are close to one another (1.5×10^{-4} and $2.6 \times 10^{-4} \text{ mol}^{-1} \text{ s}^{-1}$, respectively) [101], although the corresponding enthalpies of polymerization differ considerably (cf. Table 1.1). In connection with the latter observation it is worth noting that the calculated absolute ring strains of BL and CL are not very different [58]. Thus a difference between BL and CL polymerizabilities is related to the rate of the back, de-propagation reaction, being much more faster for BL monomer. For another pair of monomers, such as β -propiolactone (PL) and CL, the rate constants of propagation in the anionic process differ by about 10^3 -fold in favor of the less-strained CL [102].

More recently, the kinetics of polymerization of the 6-, 7-, 9-, 12-, 13-, 16 and 17-membered lactones, either initiated with a zinc 2-ethylhexanoate/butyl alcohol system [103] or catalyzed enzymatically [103, 104], have been studied. For the resultant zinc alkoxide-propagating species the following relative polymerization rates were measured: 2500, 330, 21, 0.9, 1, 0.9 and 1, respectively (bulk polymerization, 100°C). As active species operating in the polymerization of various lactones in this system are structurally identical (viz. $-\text{C}(\text{O})(\text{CH}_2)_{m-1}\text{CH}_2\text{O}-\text{Zn}-$), the order of the polymerization rates was seen to be equivalent to the order of lactone reactivities. A comparison of lactone ring size with relative polymerization rate showed that, the larger the lactone ring, the lower was its reactivity (reactivities of the 12-, 13-, 16- and 17-membered lactones were practically identical, allowing for experimental error). It might be expected that, in the transition state of propagation, lactone strain is partially released and the resultant ΔH_p^\ddagger is lower for strained

monomers compared to non-strained monomers. This, most likely, is the main reason why the reactivity of lactones decreases with their increasing sizes and eventually reaches a constant value for larger rings. Other factors, such as the electrophilicity of the monomer acyl atom or steric hindrance, both of which hamper the approach of the active species to the lactone ester group, may also play a minor role.

Interestingly, the order of enzymatic polymerization rates showed an inverted dependence on ring size, namely: 0.10:0.13:0.19:0.74:1.0 for the 7-, 12-, 13-, 16- and 17-membered lactones, respectively [103]. This kinetic behavior can be explained by assuming that, in enzymatic polymerization, the rate-determining step involves the formation of a lactone–enzyme complex. The latter reaction is promoted by the hydrophobicity of the lactone monomer, which is higher for the larger lactone rings. The conclusion reached was that, for the enzymatic process, the thermodynamic and kinetic polymerizabilities with regards to monomer ring size were in reverse sequence.

1.3.2

Kinetics of Living Polymerization

Living polymerization constitutes a particularly useful model system for conducting rigorous and systematic kinetic studies to determine the absolute rate constants of involved elementary reactions. As the kinetics of ROP has been reviewed on several occasions in the past [3a, 4, 7, 12, 23, 24, 105–107], we will at this point present only a brief summary of the most important phenomena, complemented with some recent findings.

The anionic polymerization of EO was, historically speaking, the first ROP to conform to the living polymerization criteria. As early as the 1940s, Flory had observed that the anionic propagation of EO could proceed without side reactions, such as irreversible transfer and termination [108, 109]. At the time, an analysis of this process presented by Flory pointed to the molar mass control given by the molar $([EO]_0 - [EO])/[I]_0$ ratio and a Poisson molar mass distribution of the resultant poly(EO). Some 20 years later, however, living anionic polymerization of another class of cyclic monomer, the alkylene sulfides (thiiranes), was reported [110, 111]. This discovery was followed by an establishment of the living polymerization conditions for anionic and coordination (pseudoanionic) polymerizations of lactones of various ring sizes [81, 112–116], lactams (activated monomer mechanism) [117] and, more recently, for *N*-carboxyanhydrides of α -amino acids [118–120].

During the 1970s, when the field of living cationic ROP underwent extensive development, the absolute rate constants were determined only for THF [106]. Nonetheless, a number of kinetic investigations were conducted with the cationic polymerization of substituted aziridines [121] and 1,3-oxazolines [122–124], and this in turn led to the revelation of a variety of attributes of ‘livingness’ associated with these processes.

It should also be noted that the anionic and cationic polymerization of cyclic trisiloxanes were both found to be devoid of termination and irreversible transfer, such that—in principle—the criteria of the living process were fulfilled. In contrast,

the rapid and reversible reactions which occur in the system compete effectively with propagation, such that the molar masses of the resultant siloxanes, their distribution, and the structure of the end groups cannot be precisely controlled (see Sections 2.2.2.1 and 3.3 in Ref. [12]).

1.3.2.1 Kinetic Criteria of Living Polymerization

The kinetic scheme of living, reversible ROP can also encompass—apart from initiation (Equation 1.27a) and propagation (Equation 1.27b)—additional reversible reactions, such as segmental exchange (Equation 1.27c) or temporary termination (Equation 1.27d).



where P_i^* denotes the living macromolecule, T is the deactivating agent, P_n is the temporary deactivated macromolecule, k_{tr2} is the rate constant of the bimolecular transfer to polymer with chain rupture, and k_{da} and k_a are the rate constants of temporary deactivation and activation, respectively.

In spite of the side reactions (Equations 1.27c and d) that may take place, the polymerization described by Equation 1.27 meets the criteria of the living process, provided that the activation is sufficiently fast (i.e. $k_a \geq k_p[M]$) since, under this condition, the system comprises exclusively macromolecules that are capable of growth.

In the case of rapid initiation and reversible propagation being the only reactions in the polymerizing system, and proceeding only with one kind of active center, the expression for the polymerization rate (assuming the independence of k_p on DP_n) reads:

$$R_p = -\frac{d[M]}{dt} = k_p \Sigma [P_n^*] [M] - k_d \Sigma [P_n^*] \quad (1.28)$$

Integration of Equation 1.28 leads to the well-recognized semilogarithmic dependence of monomer concentration on polymerization time:

$$\ln \frac{[M]_0 - [M]_{eq}}{[M] - [M]_{eq}} = k_p \Sigma [P_n^*] t = k_p [I]_0 t \quad (1.29)$$

For the strained three- and four-membered monomers, $[M]_{eq} \approx 0$. However, the need to insert $[M]_{eq}$ into Equation 1.29 for the higher-membered monomers seems self-evident. Moreover, the $[M]_{eq}$ value determined under the exact polymerization conditions must be used since, in the past serious errors have been made in the

kinetic analysis of THF polymerization due to incorrect values of $[\text{THF}]_{\text{eq}}$ being applied (for a more detailed discussion, see Ref. [56]). Likewise, in the example of LA polymerization conducted at an elevated temperature (e.g. 80°C, at which $[\text{LA}]_{\text{eq}} = 0.055 \text{ mol l}^{-1}$), the simplified equation $\ln([M]_0/[M]) = k_p[I]_0 t$, is occasionally used. This results in incorrect kinetic plots, especially for any relatively low concentrations of the starting monomer (e.g. $[\text{LA}]_0 \leq 1 \text{ mol l}^{-1}$).

The DP_n of the growing living polymer is a simple, linear function of monomer conversion (assuming that $k_i \geq k_p$):

$$DP_n = \frac{[M]_0 - [M]}{[I]_0} = \frac{[M]_0}{[I]_0} \times \frac{[M]_0 - [M]}{[M]_0}; \quad [I]_0 = \Sigma [P_n^*] \quad (1.30)$$

Thus, plots of $\ln\{([M]_0 - [M]_{\text{eq}})/([M] - [M]_{\text{eq}})\}$ on time and DP_n (M_n) on monomer conversion ($([M]_0 - [M])/[M]_0$) are typically used as a criterion of polymerization livingness. An example of experimental points placed on these coordinates is shown in Figure 1.8 [98].

Two sets of points are used on the kinetic plot (Figure 1.8a); one set is for conversion as measured by SEC, and the other set for conversion determined from polarimetric readings. The linearity of this plot from the very start of the polymerization points to a rapid initiation and an absence of chain termination. The molar mass evolution plot (Figure 1.8b) is also linear, and fits the theoretical line which is calculated by assuming the starting $[M]_0$ and $[I]_0$ concentrations (Equation 1.30). This result reveals the initiation to be both rapid and quantitative—that is,

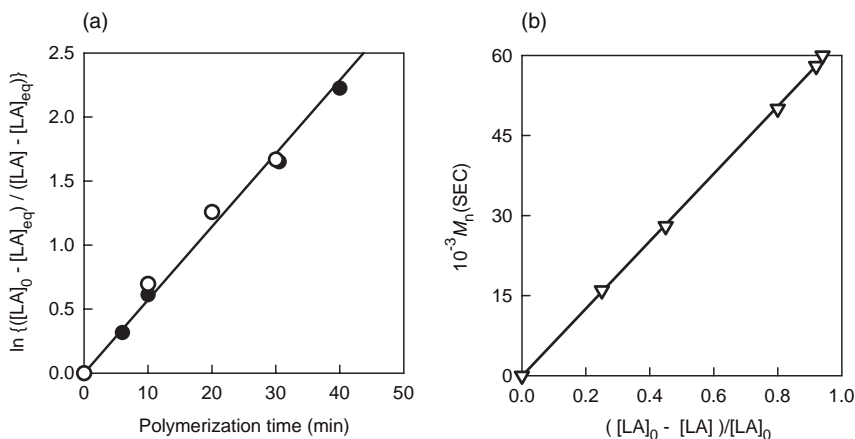
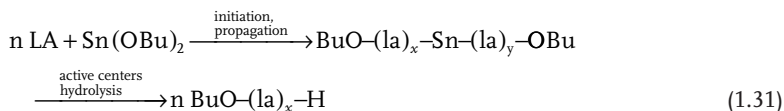


Figure 1.8 (a) Semilogarithmic kinetic plot and (b) molar masses evolution with monomer conversion, determined in the polymerization of L,L-lactide (LA) initiated with $\text{Sn}(\text{OBu})_2$. Conditions: $[\text{LA}]_0 = 1.0 \text{ mol l}^{-1}$, $[\text{Sn}(\text{OBu})_2]_0 = 1.16 \times 10^{-3} \text{ mol l}^{-1}$, THF solvent, 80°C. Concentration of $[\text{LA}]$ monitored by SEC (●) and polarimetry (○) [98].

each molecule of the difunctional initiator ($\text{Sn}(\text{OBU})_2$) begins the growth of exactly two macromolecules from one $\text{Sn}(\text{II})$ atom (Equation 1.31).



The slow initiation results typically in a positive curvature (acceleration) of the kinetic plot, but in a negative curvature for the molar mass evolution plot (see e.g. the slow initiation case in the $\text{LA}/\text{Al}(\text{O}^i\text{Pr})_3$ tetramer system [125a]). Beste and Hall [125b], and later also Pepper [125c], each described methods of trial and error analysis which allowed the determination k_i and k_p values on the basis of experimental $[\text{M}]$ versus time data (an example is provided in Ref. [125d]). More recently, however, less-cumbersome computational methods starting from kinetic Equations 1.27a and b have more often been employed (see e.g. Ref. [125a]).

Interestingly, a slow initiation does not lead to an especially broad molar mass distribution, and in this case (assuming that other reactions leading to higher polymer dispersities can be excluded), the Gold distribution is applicable. Therefore, whilst $D \leq 1.4$ can be expected even for k_p/k_i ratios higher than 10^3 [126], the molar mass of the resultant polymer can barely be controlled.

It should also be noted that termination inevitably leads to a decrease in the polymerization rate, which in turn causes a negative curvature of the kinetic plot, although this side reaction does not cause any change in the linear molar mass evolution plot.

Some time ago, the two above-discussed criteria of livingness were taken together to yield a dependence [127]:

$$-\ln\left(1 - \frac{[\text{I}]_0}{[\text{M}]_0 - [\text{M}]_{\text{eq}}} DP_n\right) = k_p [\text{I}]_0 t \quad (1.32)$$

The linearity of the $-\ln\{1 - DP_n [\text{I}]_0/([\text{M}]_0 - [\text{M}]_{\text{eq}})\}$ versus time plot, in the instance of fast initiation, provides a both necessary and sufficient criterion of livingness. The third plot, which combines the two plots from Figure 1.8, is shown in Figure 1.9. Again, the linearity of the plot corresponds to the living and controlled character of LA polymerization initiated with $\text{Sn}(\text{OBU})_2$.

1.3.2.2 Active Center Interconversions and the Determination of Absolute Rate Constants

Active centers are formed on the first addition of monomer to initiator. Since, for purposes of controlled polymerization, this step must be both rapid and quantitative, there is no need to discuss the initiation step separately at this point.

Recent methods used to determine the chemical structures and/or concentrations of active centers in ROP elaborated [23, 24] were mostly based on direct

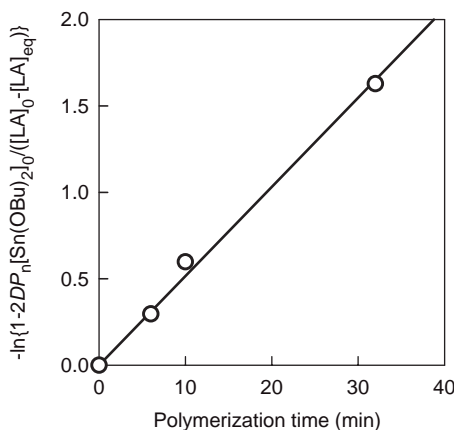


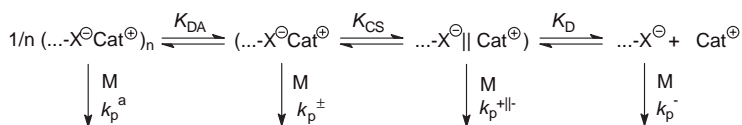
Figure 1.9 Dependence of $-\ln\{1 - 2DP_n [\text{Sn}(\text{OBu})_2]_0 / ([\text{LA}]_0 - [\text{LA}]_{\text{eq}})\}$ on time. The conditions of polymerization were as in Figure 1.8.

spectroscopic measurements of the living polymerization mixtures (e.g. ^1H NMR [128–136], ^{27}Al NMR [137]) or of end-capped structures, for example with P-containing agents (phosphines in cationic [138, 139] or diphenylchlorophosphorane in anionic polymerization [140]) by using ^{31}P NMR.

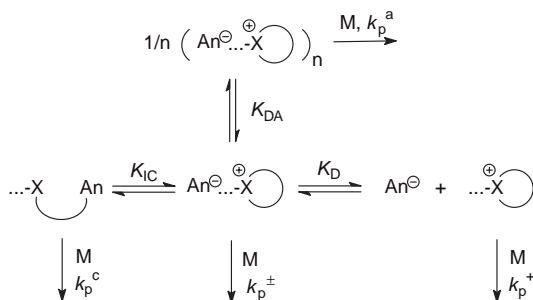
The determination of chemical structure is necessary – but not always adequate – for providing a complete description of the polymerization process. In particular, for ionic polymerization a variety of physical forms of active center exists, including (free) ions, ion pairs (contact or separated), ion pair aggregates, covalent species and their aggregates, all of which are in equilibrium [141]. Each of these structures can participate in propagation processes, with their own rate constant (Scheme 1.3). To the best of our knowledge, covalent–ionic species interconversions have been observed only in cationic polymerization [23, 24], whereas ion pair and covalent species aggregation is characteristic of anionic and coordination (pseudoanionic) processes, respectively [8b]. However, in cationic process ion pairs may also undergo aggregation at higher concentrations.

1.3.2.2.1 Reactivities of Ions and Ion Pairs Aggregation in anionic polymerization can be eliminated by the complexation of counterions with crown ethers [112] or cryptands [113]) and/or by the application of polar solvents such as hexamethylphosphotriamide (HMPT), dimethyl sulfoxide (DMSO) or dimethyl formamide (DMF) [142]. The K_D in systems devoid of ion pair aggregation can be determined from conductometric measurements [141a]. The fraction of ions (α) in the polymerizing mixture depends directly on K_D and the total concentration of ionic species (ions and ion pairs). In the living polymerization with a fast initiation, the latter is equal to the starting concentration of the initiator ($[I]_0$). The corresponding Equation 1.33 can be derived directly, starting from the expression for an ion pair–ion equilibrium constant.

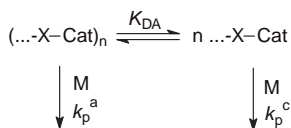
(a) Anionic polymerization



(b) Cationic polymerization



(c) Coordination (pseudoanionic) polymerization



Cat^{\oplus} , An^{\ominus} = counterions

X = heteroatom or group containing heteroatoms; M = monomer molecule.

K_{DA} , K_{CS} , K_D , K_{IC} = equilibrium constants of disaggregation, between contact and separated ion pairs, of dissociation, and of ion pair to covalent species collapse, respectively.

k_p^c , k_p^a , k_p^{\pm} , $k_p^{+||-}$ and k_p^{-} = corresponding rate constants of propagation.

Scheme 1.3 Equilibria between various structures of active species in ROP.

$$\alpha = \frac{K_D}{2[I]_0} \left(\sqrt{1 + 4 \frac{[I]_0}{K_D}} - 1 \right) \quad (1.33a)$$

$$\alpha = \sqrt{\frac{K_D}{[I]_0}} \quad (1.33b)$$

Equation 1.33b is obtained from Equation 1.33a by introducing the assumption that $[I]_0/K_D \gg 1$, which is valid for weak electrolytes.

Values of K_D for alkoxide, thiolate and carboxylate species with Li^+ , Na^+ or K^+ counterions, determined in the anionic polymerization of EO and CL, ethylene sulfide (thiirane) and PL polymerization, lie in a very broad range of values, from

$\approx 10^{-10}$ up to $\approx 10^{-4} \text{ mol l}^{-1}$ (cf. Table 3.4 in Ref. [24] and Table 4.1 in Ref. [12]). Low K_D values, which are characteristic of polymerizations conducted in THF without cation-complexing agents, increase considerably after the addition of cryptand or crown ether and/or polymerization in polar solvents. Thus, in the former case active centers are present exclusively in the ion pair form, whilst in the latter case the fraction of free ions may be considerably higher, especially for the low total concentration of active centers.

In contrast, in the cationic polymerization of cyclic ethers (e.g. THF or seven-membered oxepane), the dissociation equilibrium constants have considerably higher values, depending on the solvent polarity: $K_D \approx 10^{-5} \text{ mol l}^{-1}$ (CH_2Cl_2) and $\approx 10^{-3} \text{ mol l}^{-1}$ (CH_3NO_2 , $\text{C}_6\text{H}_5\text{NO}_2$) with SbCl_6^- as a counterion (see Table 8 in Ref. [3a]).

This pronounced difference between anionic and cationic polymerizations can be attributed to the fact that, in anionic centers, the negative charge is concentrated on the heteroatom(s), whereas in cationic centers (e.g. oxonium ions) the positive charge is located not on the oxygen atom but rather on the adjacent carbon and hydrogen atoms [143].

Thus, in ionic polymerization the results of kinetic measurements performed for a single set of conditions ($[\text{M}]_0$, $[\text{I}]_0$, solvent and temperature) and then inserted into the $\ln\{([\text{M}]_0 - [\text{M}]_{\text{eq}})/([\text{M}]_0 - [\text{M}])\}$ -time coordinates (Equation 1.29), provide only an apparent rate constant (k_p), when several types of active centers are in operation. For example, in the anionic polymerization case:

$$k_p = k_p^+ + (k_p^- - k_p^+) \alpha \quad (1.34)$$

Thus, by combining Equations 1.29, 1.33b and 1.34 one obtains:

$$k_p = k_p^+ + (k_p^- - k_p^+) \sqrt{\frac{K_D}{[\text{I}]_0}} \quad (1.35)$$

In order to determine the absolute rate constants k_p^+ and k_p^- it is necessary to measure k_p for various degrees of dissociation α (i.e. by changing $[\text{I}]_0$; see Equation 1.35). k_p^+ and k_p^- can then be evaluated from k_p on the $(K_D/[\text{I}]_0)^{1/2}$ plot, where the intercept gives k_p^+ and the slope gives $k_p^- - k_p^+$.

In anionic ROP, k_p^+ and k_p^- were determined for a number of monomer/counterion/solvent systems [24]. Results obtained for CL polymerization was typical for a majority of other systems; namely, alkoxide macroions were much more reactive than alkoxide macroion pairs: for example $k_p^- = 3.5 \times 10^2 \text{ mol}^{-1} \text{ l s}^{-1}$, whereas $k_p^+ = 4.8$ and $5 \text{ mol}^{-1} \text{ l s}^{-1}$ for the K^+ [144] and K^+ /18-dibenzo-crown-6 ether (DBC) [102] counterions, respectively (THF solvent, 20°C). Interestingly, the enthalpy of activation for the macroions $[\Delta H_p^\ddagger(-) = 39.2 \text{ kJ mol}^{-1}]$ was higher than that for macroion pairs $[\Delta H_p^\ddagger(\pm) = 13.7 \text{ kJ mol}^{-1}]$. Therefore, below a certain temperature—the temperature of inversion (T_i)—the reactivity of macroions should be lower than that of the macroion pairs (Equation 1.26). The T_i calculated from the thermodynamic parameters of activation for macroions and macroion pairs

(Equation 1.26) was equal to -64°C [102]. For PL propagating on carboxylate species with a K^+/DBC counterion in DMF as solvent, T_i was found experimentally to be equal to 20°C [142].

The plausible explanation for this striking phenomenon states that:

“... that around the macroion pair (\ominus , \oplus) solvent (S) and monomer (M) molecules ... are packed disorderly in the available space and being not oriented in any specific way. On the contrary, macroion is specifically solvated, and the thermodynamic potential of the monomer molecules solvating the active species differ from this of monomer in solution. The lower the temperature the more perfect becomes the solvation shell around ions and removal of solvent and/or monomer molecules, a necessary step preceding propagation, becomes more and more difficult. Thus, the activity of ions decreases faster with lowering temperature than the reactivity of ion pairs, where the solvation is not important. Then, at certain temperature, reactivities become equal one to another, which is followed by their inversion after further temperature decrease” [12].

A similar inversion of reactivities was also reported for thiolate active centers with alkali metal counterions complexed with cryptates, in propylene sulfide (2-methylthiirane) polymerization [111].

The absolute rate constants of propagation have also been determined in cationic ROP [145–148], although full kinetic analyses have only been performed for THF [146], oxepane [147] and conidine [148] polymerization.

In contrast to anionic ROP (and to anionic vinyl polymerization), the reactivities of macroions and macroion pairs were found to equate, within experimental error. For example, in the polymerization of THF, $k_p^+ = k_p^\ddagger = 6.0 \times 10^{-4} \text{ mol}^{-1} \text{ l s}^{-1}$ (SbCl_6^- counterion, CH_2Cl_2 , 25°C) or $4.7 \times 10^{-4} \text{ mol}^{-1} \text{ l s}^{-1}$ (SbCl_6^- , $\text{C}_6\text{H}_5\text{NO}_2$, 25°C).

The observation that for THF, $k_p^+ = k_p^\ddagger$, seems to be a general feature of cationic ROP, and at least two reasons have been proposed for this important feature to occur. As explained in Ref. [12]:

“... The first is related to the size of active species; due to the large size of anions the Coulombic attractions between cation and anion are relatively weak and the nature of anion does not affect significantly the reactivity of cation. The second explanation is based on the assumed mechanism of the propagation step. Counterion is a ‘large ball under the relatively steep roof’ and it can be further visualized that this ball (counterion) flows to the new position when the monomer adds to the oxonium ion, in which over 90% of the positive charge is

located on the CH_2 groups. This is an additional argument that the counterion does not have to be removed far away from its position in the ground state to the transition state during the propagation step, and there is no reason for the activation energies for the propagation step on ions or ion-pairs to differ substantially. Thus, $k_p^+ \approx k_p^\pm$, as found experimentally, is not surprising for these systems. In the anionic ring-opening propagation discussed earlier; the negative charge is localized (e.g. in the alkoxide anion) while the size of counteraction is usually rather small. Thus, the monomer addition requires an extensive charge separation in the ion pairs.”

Another general feature of the cationic process is that $k_p^i (= k_p^+ = k_p^\pm)$ with a given onium cation increase with increasing nucleophilicity of the monomer, whereas for a given monomer k_p^i there is a decrease with increasing nucleophilicity of the heteroatom in the onium active species. However, the observed net result is that k_p^i depends on the cyclic monomer nucleophilicity—that is, it increases in the order: amines < oxazolines < sulfides < ethers < acetals [107].

1.3.2.2.2 Kinetics of Propagation in Systems with Growing-Dormant Centers Equilibria Growing-active species equilibria (Equation 1.27d), which was first observed by Szwarc during the early 1960s in the anionic polymerization of styrene [149], play a fundamental role in polymer chemistry, as an understanding of these phenomena led to the creation of a solid base for the development of controlled cationic [150] and radical [151] vinyl polymerizations. These types of equilibria were also observed in the living ROP.

Cationic Polymerization Growing-dormant species equilibria in cationic ROP have another origin than that in anionic or coordination processes. Namely, certain ion pair counterions, such as CH_3SO_3^- , CF_3SO_3^- or ClO_4^- , react with onium cations in the active center, using two electrons of the oxygen atom to create a covalent bond. Therefore, whenever polymerization proceeds with these anions, reversible ester formation may take place (e.g. in THF polymerization with CF_3SO_3^- counterion the $-\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OSO}_2\text{CF}_3$ ester is formed) [3a, 23, 106]. The relative concentrations of macroesters and macroion-pairs in solvents of very different polarity, namely CCl_4 , CH_2Cl_2 and CH_3NO_2 , vary dramatically. There are almost no ions in CCl_4 , and almost no covalent species in CH_3NO_2 . The covalent bond formation has important consequences due to the very low reactivity of the resultant macroester species.

When the ionic (ions and ion pairs of equal reactivity, without regard for the counterion structure) and covalent species operate simultaneously, such that the apparent rate constant (k_p) is a resultant of the absolute rate constants k_p^i and k_p^c and proportions of ionic (β) and covalent species ($1-\beta$):

$$k_p = \beta k_p^i + (1 - \beta) k_p^c \quad (1.36)$$

The k_p is determined experimentally from the $\ln\{([M]_0 - [M]_{eq})/([M] - [M]_{eq})\}$ on time plot (Equation 1.29). If the proportions of ionic and covalent species are known (for example, from ^1H NMR measurements [128]), then k_p^c may be determined from one kinetic run. In the polymerization of THF performed in solvents of different polarity, the following k_p^c values were determined: $6 \times 10^{-5} \text{ mol}^{-1} \text{ s}^{-1}$ (CCl_4) and $5 \times 10^{-4} \text{ mol}^{-1} \text{ s}^{-1}$ (CH_3NO_2) ($[\text{THF}]_0 = 8 \text{ mol l}^{-1}$, 25°C) [56]. In concluding, the reactivity of covalent species is approximately three orders of magnitude lower than that of ionic species, and therefore the ionic species, even if present in a small fraction, are almost exclusively responsible for the propagation. The results of recent studies with of 2-methyl oxazoline cationic polymerization have led to similar conclusions [124].

A complete description of the cationic polymerization of THF, including all rate constants for the ionic and covalent species interconversions, and methods of their determination, may be found in Chapter 5 of Ref. [3a]. For a more concise description, however, see Section 3.1.1 in Ref. [12].

Anionic and Coordination Polymerization Aggregates of ion pairs, or of covalent species formed reversibly in the anionic or pseudoanionic polymerization of EO [152, 153], cyclosiloxanes [154] and cyclic esters [79, 155–157], were found to be essentially unreactive; thus, in polymer chain growth only unimeric, deaggregated species will participate. The pertinent kinetic scheme reads:



A solution of the kinetics shown in Equation 1.37 provides two useful dependences [155, 156]:

$$\ln r_p = \ln k_p (mK_A)^{-1/m} + \frac{1}{m} \ln [I]_0 \quad (1.38a)$$

$$r_p^{1-m} = -mK_A k_p^{1-m} + k_p [I]_0 r_p^{-m} \quad (1.38b)$$

where $r_p = d[M]/[M]dt = t^{-1} \ln([M]_0/[M])$, and $[I]_0$ is the starting concentration of initiator [this is equal, at the correctly chosen (living) conditions, to the total concentration of active centers, both growing and dormant (for CL at room temperature $[M]_{eq} \approx 0$)].

Fitting the experimental data (i.e. r_p and $[I]_0$) available from the kinetic measurements to Equation 1.38a allows determination of the degree of aggregation (m).

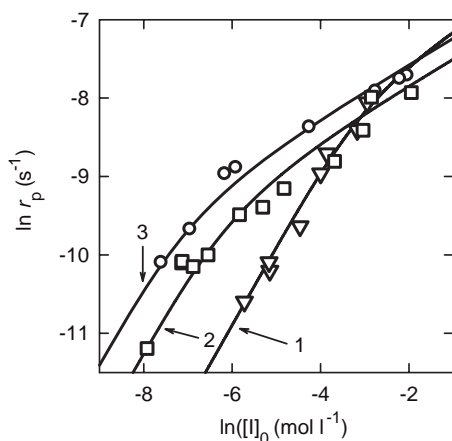


Figure 1.10 External order of initiator dependencies (Equation 1.37a) obtained in polymerization of ϵ -caprolactone (CL) initiated with Et_2AlOEt . Conditions: $[\text{CL}]_0 = 2 \text{ mol l}^{-1}$, solvents: CH_3CN (curve 1), THF (curve 2), C_6H_6 (curve 3); temperature 25°C . The points represent experimental data; the lines were computed numerically, assuming kinetic Equation 1.37a–c [157].

Figure 1.10 shows an example of the r_p versus $[\text{I}]_0$ dependencies (Equation 1.38a) obtained in the polymerization of CL initiated with Et_2AlOEt and carried out in CH_3CN , THF and C_6H_6 as solvents [157]. The resultant plots reveal that the order in initiator in all solvents decreases from 1 to 1/3 with increasing total concentrations of active centers (equivalent to $[\text{I}]_0$ in the living polymerization conditions). This behavior points clearly to the aggregation of unimeric aluminum alkoxide ($-\text{C}(=\text{O})\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O}-\text{AlEt}_2$) active centers into the unreactive trimers.

Unfortunately, this approach does not allow the separate determination of K_a and k_p , but only their product. A method to determine both k_p and K_a is possible, however, particularly when the degree of aggregation can be estimated in the manner described above. For this, Equation 1.38b provides a direct access to both k_p and K_a . The power of this analytical approach can be seen by comparing the two figures taken from Ref. [105] (Figure 1.11).

Although the degree of aggregation has long been known to equal 3 for polymerizations conducted with diethyl aluminum alkoxide, a decision was taken also to check results when deliberately introducing an incorrect aggregation number of 2. The resultant plot produced highly dispersed points, unlike the typical straight line obtained with a value of 3.

Values of k_p and K_a determined for the CL/ Et_2AlOEt system in solvents of various polarities and solvating power are collected in Table 1.2. These data reveal that, the higher dielectric constant of the solvent, the lower are both k_p and K_a . Namely, an increase in ϵ from 2.3 to 37 causes a decrease in k_p from 8.6×10^{-2} to $7.5 \times 10^{-3} \text{ mol}^{-1} \text{ l s}^{-1}$ (i.e. 11-fold) and a simultaneous decrease in K_a , from 2.4×10^5

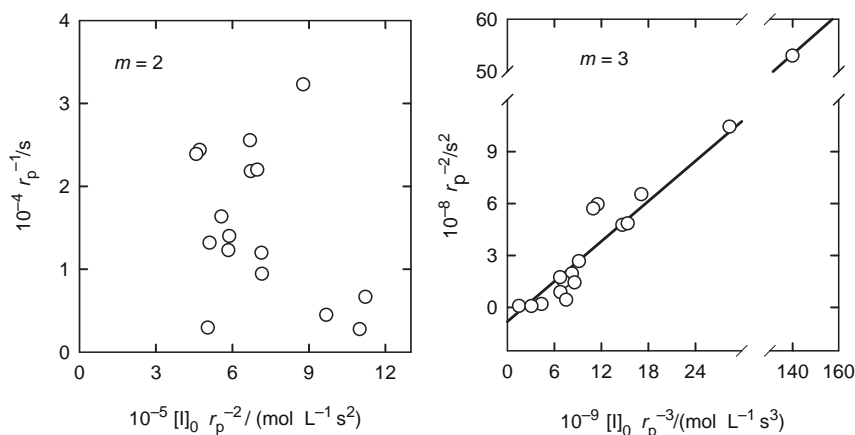


Figure 1.11 Polymerization of ϵ -caprolactone (CL) initiated with Et_2AlOEt (THF, 25°C). Test of Equation 1.37b for degree of aggregation, m . Only for $m = 3$ was a straight line obtained as required. (The primary kinetic data were taken from Ref. [156].)

Table 1.2 Absolute propagation rate constants (k_p) and equilibrium constants of aggregation (K_A) for polymerization of ϵ -caprolactone initiated by diethylaluminum ethoxide^a [157]

Solvent	Dielectric constant (ϵ)	$\frac{k_p}{\text{mol}^{-1} \text{L s}^{-1}}$	$\frac{K_A}{\text{mol}^{-2} \text{L}^2}$
CH_3CN	37	7.5×10^{-3}	7.7×10^1
THF	7.3	3.9×10^{-2}	5.5×10^4
C_6H_6	2.3	8.6×10^{-2}	2.4×10^5

^a $[\text{CL}]_0 = 2 \text{ mol l}^{-1}$, 25°C .

to $7.7 \times 10 \text{ mol}^{-2} \text{L}^2$. Therefore, for the lower total concentrations of active centers when the nonaggregated, actually growing species dominate (Figure 1.10), the polymerization rates order, measured for a given $[\text{I}]_0$ is as follows: $r_p(\text{C}_6\text{H}_6) > r_p(\text{THF}) > r_p(\text{CH}_3\text{CN})$. However, for a higher $[\text{I}]_0$, when the concentration of the unreactive aggregates increases, and this increase is stronger for the less-polar solvents, the polymerization rates tend to converge, such that at $[\text{I}]_0 = 0.1 \text{ mol l}^{-1}$ the r_p -values measured in C_6H_6 , THF and CH_3CN become almost identical (Figure 1.10). CH_3CN is the most polar of the three solvents used, and apparently breaks down the aggregates. Thus, within the studied range of concentrations the active species are mostly unimeric (i.e. reactive). In both THF and C_6H_6 the equilibrium

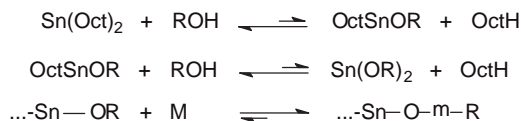
between aggregated (unreactive-dormant) and nonaggregated species persists, although at the sufficiently low concentration for a given system the fraction of aggregated species may be negligibly small and no longer important. Both, the alkoxide active center and lactone molecule have dipolar structures. An analysis of the influence of the solvent dielectric constant, as the macroscopic parameter, on the k_p (the dipolar molecule–dipolar molecule reaction) in terms of the electrostatic effects, shows that increase in ϵ should lead to a higher value of k_p . In the analyzed case, however, a reverse order is observed, namely k_p in CH_3CN is lower than in THF and benzene. Such behavior may be related to the specific solvation of the growing dialkylaluminum alkoxide by the dipolar solvents (i.e. THF, CH_3CN), both of which are sufficiently strong in their ground state, and increase ΔH_p^\ddagger in this way. It appears that these specific solvation effects prevail over the electrostatic field effects, with the net result being a decrease in k_p while increasing polarity and solvating power of the solvent is observed.

The exchange rates between aggregated (dormant) and unimeric (propagating) species in the CL/ R_2AlOR system are sufficiently high as to govern even the growth of all macromolecules, as can be judged from the M_w/M_n values determined for the resulting poly(CL) being in the range from 1.03 to 1.13 [116].

Equation 1.38b allows k_p and K_a to be determined for several other systems (including the anionic polymerization of EO and D₃), that previously had been analyzed using numerical calculations [158]. Szwarc *et al.* indicated that such an analytical solution should exist, and discussed in more detail the problems of aggregation in anionic polymerizations and the related kinetic consequences [159].

It is worth adding at this point that, in the context of the aggregation phenomena observed in propagation, some initiators which are applied in the coordination polymerization, and eventually are transformed into the covalent active species, are known to exist mostly in the aggregated (dormant) forms. For instance, $\text{Al}(\text{O}^i\text{Pr})_3$ is known to form both trimeric (A_3) and tetrameric (A_4) aggregates; subsequent ^1H NMR and kinetic measurements revealed that, in the polymerization of CL [160, 161] initiated with a mixture of A_3 and A_4 at ambient temperatures, the trimeric aggregate exclusively initiated polymerization. The ratio of the corresponding initiation rates ($k_i(A_3)/k_i(A_4)$) was estimated as equal to 10^3 , with the propagation being complete before the tetrameric $\text{Al}(\text{O}^i\text{Pr})_3$ reacts to any observable degree. When polymerization comes to the living polymer–monomer equilibrium, the mostly unreacted A_4 is introduced slowly into the polymer chains via alkoxide-ester group transesterification reactions. Eventually, therefore, due to these segmental exchange reactions between living macromolecules, there is only one population of macromolecules having the most probable distribution of molar masses.

When the A_3/A_4 mixture is used to initiate polymerization at a sufficiently high temperature—that is, under conditions where the rate of interexchange between A_3 and A_4 is at least as fast as initiation with A_4 —the aggregation phenomena become of minor importance. This type of situation will occur in LA polymerizations carried out above 100°C [125].



Oct = O(O=)CCH(C₂H₅)C₄H₉

RO = (macro)alkoxy group

Scheme 1.4 Mechanism of cyclic esters polymerization initiated by Sn(II) octoate.

Sn(II) Octoate-Initiated Polymerization In a series of kinetic studies it has been shown that, during processes employing tin octoate [Sn(Oct)₂] (Sn[O(O=)CCH(C₂H₅)C₄H₉]₂), the actual initiator and then the active center–Sn(II) alkoxide is formed reversibly in the alkoxy–carboxylate ligand interexchange reaction at the Sn atom (Scheme 1.4) [162–169]. The (macro)alcohol species can therefore be treated as being temporarily terminated dormant.

The formation of Sn(II) alkoxide from Sn(Oct)₂ and an alcohol is a reversible reaction. Although the rates of exchange and the position of equilibria have not yet been established, the activation–deactivation reactions must be relatively rapid since, for up to ≈80% of the monomer conversion at 80°C in THF solvent the *M_w*/*M_n* dispersity index is less than 1.2 [169], while the molar masses of polyester can be predicted from the ([M]₀ – [M])/[ROH]₀ ratio [162, 163]. The influence of this interconversion on the polymerization kinetics can be approached in two ways, as shown in Scheme 1.4.

The example shown in Figure 1.12 compares the rates of LA polymerization in two systems: one system initiated with Sn(Oct)₂/BuOH, and another with Sn(OBu)₂/OctH [98]. Polymerization with [Sn(Oct)₂]₀ = 0.05 mol l^{–1} but without added alcohol is very slow (plot 1), and is coinitiated by compounds containing hydroxyl groups (which adventitiously are present in the system as impurities). Polymerization initiated with [Sn(OBu)₂]₀ = 0.05 mol l^{–1} was 2.4 × 10² times faster than that with Sn(Oct)₂ ‘alone’ (plot 4). In the next two experiments, the [Sn(Oct)₂]₀ and [Sn(OBu)₂]₀ were equal, while 0.05 mol l^{–1} and 0.1 mol l^{–1} of BuOH and OctH were added, respectively. As shown in plots 2 and 3 of Figure 1.12, the polymerization rates in the Sn(Oct)₂/BuOH and Sn(OBu)₂/OctH systems were practically the same, thereby strongly supporting the proposed polymerization mechanism noted in Scheme 1.4.

It should be added (notably with regards to the discussions in Sections 1.3.2.1 and 1.3.2.2) that, in the vast majority of recently reported kinetic studies of the ROP of heterocyclic monomers, the first internal order in monomer was observed; that is, the experimental plots of ln{([M]₀ – [M]_{eq})/([M] – [M]_{eq})} versus time were linear (Equation 1.29). Atypically, in LA polymerization initiated with zinc alkoxide bearing 2-(2-methoxyphenyl)amino-4-(2-methoxyphenyl)imino-2-pentene bidentate ligand, the second internal order in LA was observed (based on linearity of the (1/[LA]) – (1/[LA]₀) versus time plot). However, the mechanistic explanation of this result has not been provided [170a].

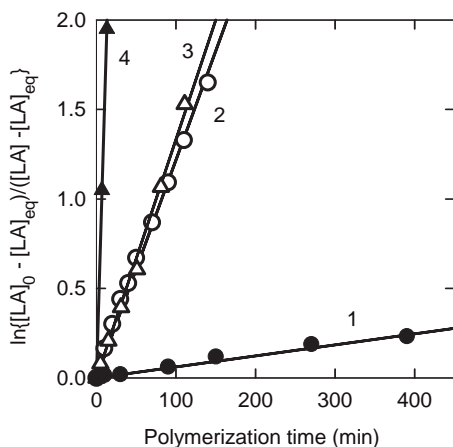


Figure 1.12 Comparison of kinetics of L,L-lactide (LA) polymerization initiated by tin octoate ($\text{Sn}(\text{Oct})_2$) (line 1), $\text{Sn}(\text{Oct})_2/\text{BuOH}$ (line 2), $\text{Sn}(\text{OBu})_2/\text{octanoic acid}$ (OctH) (line 3) and $\text{Sn}(\text{OBu})_2$ (line 4). Conditions: $[\text{LA}]_0 = 1.0 \text{ mol l}^{-1}$, $[\text{Sn}(\text{OBu})_2]_0 = [\text{Sn}(\text{Oct})_2]_0 = 0.05 \text{ mol l}^{-1}$, $[\text{OctH}]_0 = [\text{BuOH}]_0 = 0.10 \text{ mol l}^{-1}$, THF solvent, temperature 50°C [98].

Most often, the external orders in initiator $m \leq 1$ have also been reported. As discussed above, $m = 1$ corresponds to a propagation on one type of active center of a given reactivity formed quantitatively from an initiator, whereas $m < 1$ can be related to aggregation into species of lower reactivity than that of the unimeric, nonaggregated species (Equation 1.38a; $r_p \sim [\text{I}]_0^{1/m}$) or the dissociation of ion pairs into the otherwise more reactive ions (Equations 1.29 and 1.35 for $k_p^- \gg k_p^+$ give $r_p \sim [\text{I}]_0^{1/2}$).

An external order in initiator $m > 1$ poses certain interpretive problems. One possibility is that aggregates are more reactive than the parent unimeric species. Another explanation was proposed in Ref. [170b], though this stated that a certain concentration of adventitiously present impurities must be subtracted from $[\text{I}]_0$, allowing the value of $m = 1$ to be obtained. In contrast, in a situation when DP_n is easily predictable from the $([\text{M}]_0 - [\text{M}])/[\text{M}]_0$ ratio, the latter solution could not easily be accepted.

1.3.2.3 Departure from Livingness: Kinetics of Selected Side Reactions

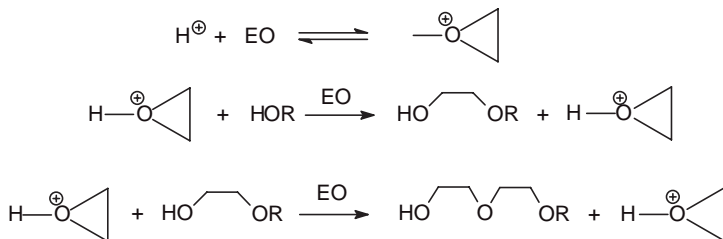
1.3.2.3.1 Cationic Polymerization The kinetics of termination, chain transfer and macrocyclization processes in cationic ROP have been extensively reviewed in Chapter 5 of Ref. [3a] and also in Ref. [74]. Of particular value is Table 18 in Ref. [3a], which details the basic equations in nonstationary kinetics with chain transfer. Although, since these two reviews were published few new phenomena have been identified, we will at this point provide a brief description of activated monomer cationic polymerization.

In cationic polymerization, the chain-transfer side reactions cannot be avoided because nucleophilic sites of the monomer molecules (heteroatoms) are still present along the chain. Indeed, in some cases (e.g. cyclic acetals: dioxolane or trioxane) the nucleophilicity of an oxygen atom is higher when located in a polymer chain than when in a monomer molecule. As mentioned in Section 1.2.3, one particularly undesirable reaction is that of back-biting, which leads to the macrocyclics fraction (see Scheme 1.1). The extent of the back-biting reaction depends on the relative nucleophilicities of the heteroatom in a monomer molecule and in polymer unit, as well as on steric factors. In the polymerization of THF, the back-biting is slow when compared to propagation, and thus the macrocyclics fraction can easily be eliminated in a kinetically controlled synthesis [3b]. In contrast, in the cationic polymerization of EO, the typically predominant product is a cyclic dimer (1,4-dioxane), whereas in the cationic polymerization of substituted oxiranes (propylene oxide, epichlorohydrin), other cyclic oligomers (trimers, tetramers) are formed in significant amounts.

During the early 1980s, the cationic polymerization of cyclic ethers in the presence of low-molecular-weight diols as chain-transfer agent was studied with the aim of preparing polyether diols [82]. A more detailed investigation of this process revealed that the addition of alcohols to the polymerization of some oxiranes reduced the proportion of cyclics which was known to be formed by back-biting. The explanation for this observation was based on the activated monomer (AM) mechanism shown in Scheme 1.5 [171, 172].

In polymerization proceeded by an AM mechanism, the active centers are located on the monomer molecule (thus activated monomer), while the growing polymer chain is neutral, despite terminating with a reactive hydroxyl group. Because in the cationic AM mechanism there is no active species at the chain end, the back-biting is greatly reduced.

Even if the AM mechanism operates in a cationic polymerization of oxiranes in the presence of hydroxyl groups, it does not eliminate the possible contribution of a conventional active chain end (ACE) mechanism (active center; oxonium ion located at the macromolecular chain end). In order for an AM-type propagation to prevail, the instantaneous concentration of monomer should be kept as low as possible (e.g. via continuous slow monomer addition).



counterion omitted

Scheme 1.5 Polymerization of ethylene oxide (EO) according to the activated monomer mechanism.

The kinetic studies, which were based exclusively on the determination of monomer consumption, allowed only an apparent rate constant to be determined (Equation 1.39).

$$-\frac{d[M]}{dt} = k_p^{\text{app}} [H-M^+][HOR]_0 \quad (1.39)$$

where $H-M^+$ denotes a protonated monomer and $[HOR]_0$ the starting alcohol concentration.

At low monomer conversion (almost no polymer present) it may be assumed that protons are distributed between oxygen atoms of monomer and hydroxyl groups only:

$$[H-M^+][^+H_2O \dots] = K_e \frac{[HOR]_0}{[M]} \quad (1.40)$$

In such a case, the sum of concentrations of protonated species is equal to the protonic acid concentration in the feed. Finally, combining Equations 1.39 and 1.40 gives Equation 1.41.

$$\frac{[H^+]}{d[M]/dt} = \frac{1}{k_p^{\text{app}}} + \frac{K_e}{k_p^{\text{app}}} \frac{[HOR]_0}{[M]} \quad (1.41)$$

Thus, by plotting the results of the kinetic measurements ($[H^+]/d[M]/dt$) at early stages of polymerization on various $[ROH]_0/[M]$ ratios, we have a direct access to both k_{app} and K_e [173, 174]. More detailed information on AM kinetics are available in a recent review (and references cited therein) [172].

1.3.2.3.2 Anionic and Coordinated Polymerization The alkoxide active centers in the polymerization of oxiranes, and carboxylate active centers in the polymerization of β -lactones, are not only nucleophilic but also sufficiently basic to abstract protons from the monomer molecule, and this eventually results in an irreversible chain transfer to monomer.

The transfer to monomer makes impossible the anionic polymerization of propylene oxide (PO; 2-methyl oxirane) to a high-molar-mass polymer (see e.g. Ref. [175] and references cited therein). However, it has been shown recently that the polymerization of PO initiated with alkaline metal alkoxides in hydrocarbon solvents can be accelerated substantially in the presence of a more than threefold molar excess of trialkylaluminum (AlR_3), with regards to the alkoxide initiator. The chain transfer is also strongly reduced, and this allows the controlled preparation of poly(PO) up to $M_n \geq 2 \times 10^4$. The role of the added AlR_3 was explained by assuming activation of both the PO monomer and the alkoxide growing species, and in this way the selectivity of the propagation versus transfer (k_p/k_{tr}) could be increased [176].

The anionic polymerization of β -substituted, four-membered lactones (e.g. BL) with alkaline metal counterions also suffers from a proton-abstraction side

reaction, leading to a chain transfer to polymer [177, 178]. The application of Bu_4N^+ as a counterion resulted in an enhancement of the k_p/k_{tr} ratio and allowed the preparation of poly(BL) with $M_n \leq 2 \times 10^5$, although the molar masses could barely be controlled [179]. Kinetic studies, supported by M_n measurements which allowed determination of the selectivity parameter $k_p/k_{tr} = 4 \cdot 10^4$ for PL (K^+/DBC , CH_2Cl_2 solvent, 20°C), and $k_p/k_{tr} \leq 2.0 \cdot 10^2$ for BL (K^+/DBC , THF solvent, 20°C) [178]. Both electronic and steric effects of the methyl group proved to be responsible for a lower value of the k_p/k_{tr} ratio in BL, when compared to PL, an effect which was due (at least partially) to differences in the rate constants of propagation (4×10^{-3} and $10^{-6} \text{ mol}^{-1} \text{ s}^{-1}$ at 20°C in THF solvent, respectively).

The anionic polymerization of cyclic esters with higher-membered ring sizes (five and more) proceeds on the alkoxide active centers. Less-nucleophilic carboxylates are unable to initiate the polymerization of these weakly or medium strained monomers, while the relatively high nucleophilicity of the alkoxides gives rise to chain transfer to polymer with chain rupture side reactions (see Scheme 1.1). As discussed earlier in Section 1.2.3, only an intramolecular transfer will lead to a departure from livingness. The kinetic scheme of polymerization accompanied by chain-transfer reactions is shown in Equation 1.42a–c.



The intramolecular process is relatively easy to study quantitatively, mainly because the products of the chain transfer are cyclic compounds, the concentration of which can be measured by using standard chromatographic methods. Thus, the propagation (Equation 1.42a) and formation of cyclic oligomers (1.42b) are competitive reactions which take place simultaneously.

Solution of the kinetic Equation 1.42 (taking into account only propagation and intramolecular transfer) for some monomers (e.g. CL) for which propagation is practically irreversible, gives Equation 1.43 [81].

$$\beta = \frac{k_p}{k_{tr1}(y)} = \frac{\ln([M(1)]_0/[M(1)])}{[M(y)]_{eq} \cdot \ln\left\{[M(y)]_{eq}/([M(y)]_{eq} - [M(x)])\right\}} \quad (1.43)$$

where $\beta = k_p/k_{tr1}(y)$ is the selectivity parameter showing how many elementary acts of propagation (at $[M(1)] = 1 \text{ mol l}^{-1}$) are accompanied by one macrocyclization. In this way, the value of β is a direct measure of selectivity of a given active center.

By using the described kinetic approach, the ratios of k_p/k_{tr1} were determined for a few initiating systems [95], whereby the ratio was seen to differ by a factor of up to 10^3 . The corresponding data are collected in Table 1.3. Here, two phenomena are involved, namely reactivity and steric hindrance. It is found that, the higher

Table 1.3 Propagation rate constants (k_p) and the selectivity parameters ($\beta = k_p/k_{tr1}$) for the polymerization of ϵ -caprolactone [95]^a

Active species	$\frac{k_p}{\text{L mol}^{-1} \text{s}^{-1}}$	$\beta = \frac{k_p/k_{tr1}}{\text{L mol}^{-1}}$
$\dots\text{-(CH}_2)_5\text{O}^-\text{Na}^+$	≥ 1.70	1.6×10^3
$\dots\text{-(CH}_2)_5\text{O-Sm[O(CH}_2)_5\text{]}_2$	2.00	2.0×10^3
$\dots\text{-(CH}_2)_5\text{O-Al(C}_2\text{H}_5)_2$	0.03	4.6×10^4
$\dots\text{-(CH}_2)_5\text{O-Al[CH}_2\text{CH(CH}_3)_2\text{]}_2$	0.03	7.7×10^4
$\dots\text{-(CH}_2)_5\text{O-Al[O(CH}_2)_5\text{]}_2$	0.50	3.0×10^5
$\dots\text{-(CH}_2)_5\text{O-AlO}_2\text{SB}^b$	0.35	$\approx 10^6$

a Polymerization conditions: 20 °C, THF solvent.

b Polymerization conditions: 80 °C, THF solvent, SBO₂: (S)-(+)-2,2'-[1,1'-binaphthyl-2,2'-diylbis-(nitylromethylidyne)]-diphenolate ligand (A. Duda and A. Kowalski, unpublished results). SB = Schiff's base.

the reactivity for species of comparable steric hindrance around growing species (e.g. Sm trialkoxide and Al trialkoxide), the lower the selectivity—as is often the case with other chemical reactions. If, on the other hand, the reactivity in propagation is the same but steric hindrance differs, then for higher sterically hindered species the selectivity is higher; this is the case with dialkylaluminum alkoxides. The best selectivity, however, was observed for a low-reactive Al alkoxide bearing a sterically demanding bidentate ligand, (S)-(+)-2,2'-[1,1'-binaphthyl-2,2'-diylbis-(nitylromethylidyne)]-diphenolate. Due to the high selectivity, it was possible to prepare the well-defined LA/CL block copolymers by initiating CL polymerization with the living poly(LA) block [180]—an approach that previously was impossible, even when using the highly selective Al trialkoxide.

The rate constant of intermolecular transfer (k_{tr2}) or, alternatively, the k_p/k_{tr2} ratio, can be determined on the basis of a change in molar mass distribution as a function of monomer conversion. First, the dependencies of M_w/M_n on $([M]_0 - [M])/[M]_0$ were computed numerically, assuming the corresponding kinetic scheme (Equation 1.42a and c) and various k_p/k_{tr2} values and starting concentrations ($[M]_0$ and $[I]_0$). The fitting of these simulated dependencies to the experimental data was then carried out, after which the k_p/k_{tr2} ratio was determined by choosing the best-fit curve [95–97, 99].

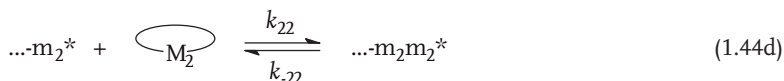
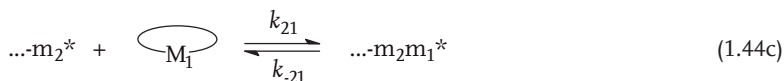
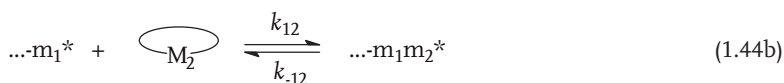
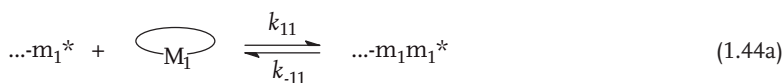
Figure 1.7 provides an example of such determinations for the LA/Sn(OBu)₂ system. The dotted and solid lines were computed assuming $k_p/k_{tr2} = 125$ and 200,

respectively. These values point to the relatively high selectivity of the Sn(II) alkoxide active centers [98].

1.3.2.4 Kinetics of Copolymerization

Typically, the kinetics of ring-opening copolymerization is analyzed in terms of the four equations, set with all reactions being irreversible. The aim of a such an analysis is to determine the reactivity ratios: $r_1 = k_{11}/k_{12}$ and $r_2 = k_{22}/k_{21}$ by means of the approaches elaborated by Mayo and Lewis or Fineman and Ross, or perhaps by Kelen and Tudos. Provided that the homopolymerization rate constants (k_{11} and k_{22}) are known from the homopolymerization studies, under otherwise identical conditions—and assuming that the same values are valid in copolymerization (this is not necessarily true for ionic or coordination ROP)—the cross-propagation rate constants (k_{12} and k_{21}) can eventually be determined.

However, with the exception of copolymerization of the three- and/or four-membered comonomers, the copolymerization of higher rings is expected to be reversible, such that four additional homo- or cross-depropagation reactions must be added (kinetic Equation 1.44). In such a situation, the traditional methods of kinetic analysis must be put ‘on hold’, as a numerical solving of the corresponding differential equations is necessary. Moreover, depending on the selectivity of the active centers, any reversible transfer reactions can interfere to various degrees with the copolymerization process. Thus, the kinetically controlled microstructure of the copolymer may differ substantially from that at equilibrium (cf. Section 1.2.4).



Instructive example of the copolymerization involving monomer propagating reversibly comes from the L,L-lactide (LA)/ ϵ -caprolactone (CL) comonomers pair [181, 182]. Recent analysis of this copolymerization system, by means of the numerical integration method [183], revealed that the comonomers reactivity ratios can be controlled by the configuration of the active species [184]. Thus, using initiator of various stereochemical compositions a broad spectrum of copolymers

having different microstructures: from gradient to more random could be prepared in a controlled way.

1.4

Concluding Remarks

In this chapter we have shown that studies of the thermodynamics and kinetics of ROP play an indispensable role in our understanding of polymerization mechanisms. The results of these investigations have helped to establish controlled polymerization conditions, allowing the preparation of polymers with required molar masses and microstructures. The presence of various heteroatoms within the macromolecular main chain introduces an almost infinite number of possible homopolymeric and copolymeric properties. A recent development has been the controlled synthesis of aliphatic polyesters, mostly via ROP, based on their potential applications as biodegradable thermoplastics or as biomedical polymers. Moreover, as some cyclic ester monomers are prepared from renewable resources, some of the examples provided here have related to the ROP of aliphatic cyclic esters.

Within the field of ROP there remain many unanswered questions, including the controlled synthesis of high-molar-mass poly(β -butyrolactone) with a sufficiently reactive yet selective initiator, the use of 'fast initiators' in lactide polymerization that function with high selectivity in the monomer/polymer melt, and identification of the mechanisms of organocatalytically prompted polymerizations. It is clear that the resolution of these problems will require a systematic and careful approach to kinetic studies.

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2

General Mechanisms in Ring-Opening Polymerization

Takeshi Endo

2.1

Introduction

The family of cyclic monomers is known to be extremely large, leading to a wide range of systems for ring-opening polymerizations (ROPs). Most of the cyclic monomers are heterocycles, the highly polarized nature of which allows them to undergo heterolysis of functional group in the ring. Therefore, numerous nucleophiles and electrophiles can react with them to initiate their ionic polymerizations. Besides this remarkable variety of ionic ROP processes, free-radically initiated ROP is also important because, potentially, it provides the opportunity to design copolymerizations of cyclic monomers and vinyl monomers. Another important class of ROP reactions relies upon the ring-opening metathesis polymerization (ROMP) of unsaturated alicyclic compounds, which affords amorphous and transparent polymers having cycloaliphatic moieties. The details of ROMP, including its mechanism, are discussed in Chapter 8.

In this chapter, some important and fundamental mechanisms for ROP are discussed and illustrated by showing some selected relevant examples. In addition, some advanced designs of more specific ROP processes are briefly introduced.

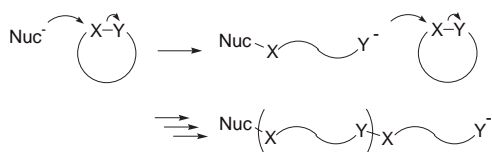
2.2

Anionic Ring-Opening Polymerization

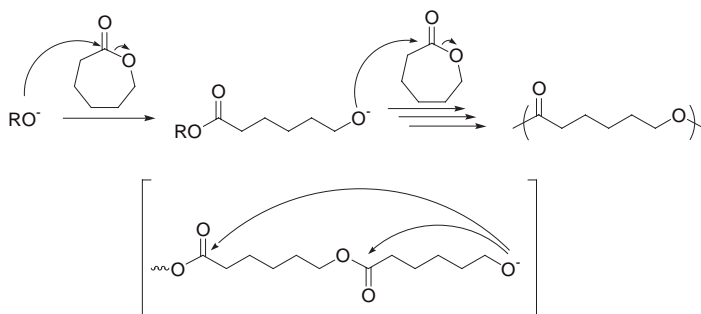
2.2.1

General Mechanism

Ring-opening polymerizations using nucleophilic reagents as initiators can be categorized into ‘anionic ROP’, a general mechanism for which is shown in Scheme 2.1. Nucleophilic reagents applicable to initiation most often involve organometals (alkyl lithium, alkyl magnesium bromide, alkyl aluminum, etc.), metal amides, alkoxides, phosphines, amines, alcohols and water. Monomers



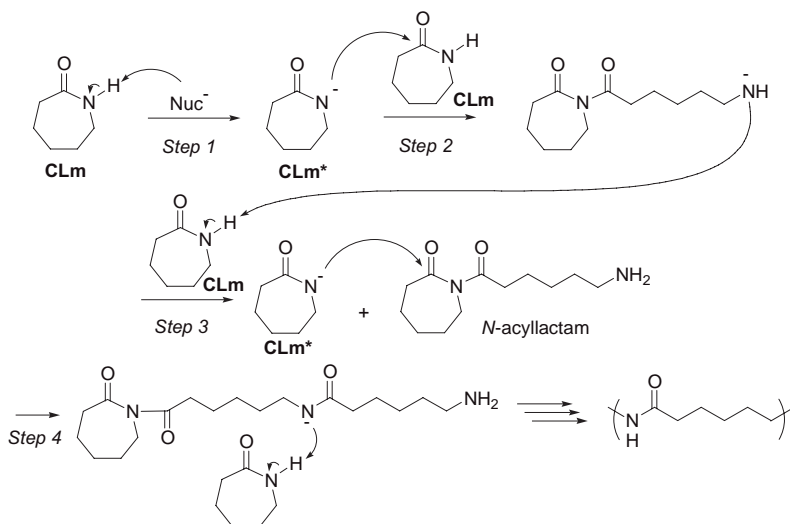
Scheme 2.1



Scheme 2.2

capable of undergoing anionic ROP possess polarized bonds such as ester, carbonate, amide, urethane and phosphate, which allow generation of the corresponding polyester, polycarbonate, polyamide, polyurethane and polyphosphate, respectively. When the monomers have a three-membered ring structure, the ring-distortion allows them to undergo ROP even though they have less-electrophilic functions such as ether, amine and thioether. These monomers include epoxide, aziridine and episulfide, which also represent other highly important cyclic monomers for practical applications. The polarized functional group in cyclic monomers will be represented by $\text{X}-\text{Y}$, where the atom X (usually, carbon atom) is becoming electron-deficient due to the highly electron-withdrawing nature of the atom Y (oxygen, nitrogen, sulfur, etc.). Thus, the ring-opening reaction of the monomer will be triggered by a nucleophilic attack of the initiator to the atom X , thereby releasing Y^- . This newly formed nucleophilic species will attack the atom X in another monomer molecule, and the repeated sequence of this process provides the corresponding polymer.

As a typical example of this type of ROP—that of ϵ -caprolactone, as initiated by an alkoxide function—is shown in Scheme 2.2 [1, 2]. Here, the alkoxide initiator reacts with the lactone at its carbonyl carbon, and this reaction leads to the formation of an alkoxide at the propagating chain end, which successively reacts with another lactone molecule. However, this propagating step is usually accompanied by side reactions, mostly represented by the terminal alkoxide back-biting of the ester linkage in the main chain of the formed polyester. This back-biting reaction gives the monomer as well as macrocyclic oligomers.



Scheme 2.3

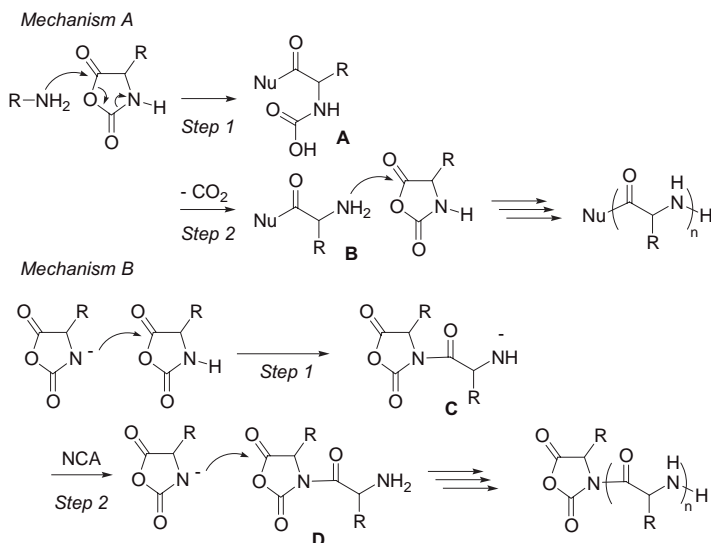
2.2.2

Activated Monomer Mechanism

The aforementioned mechanism for anionic ROP relies on ‘nucleophilic attack of propagating chain end to monomer’. In contrast, the next topic is ‘nucleophilic attack of activated monomer to polymer chain end’, which is normally referred to as ‘activated monomer mechanism’ [3].

It is well known that ϵ -caprolactam (CLm), a seven-membered cyclic amide, undergoes ROP by using an alkali metal or alkyl alkali metal as the polymerization activator [4, 5]. However, the mechanism proposed for this is less simple than that proposed for the anionic ROP of lactones. As shown in Scheme 2.3, Step 1 involves the abstraction of an acidic N-H proton from CLm under highly basic conditions. The ionized monomer—that is, the activated monomer, CLm*—attacks another molecule of lactam to induce its ring-opening reaction while releasing a highly basic amide anion (Step 2). This anion activates CLm by abstracting its N-H proton to give CLm* (Step 3), which in turn will react with the N-acylated lactam moiety in the chain end of the polymer (Step 4). The resulting species is anionic in nature, and capable of acting as a base to activate the monomer.

The next example is the ROP of amino acid-derived *N*-carboxyanhydride (NCA) (Scheme 2.4) [6–8]. As might be expected from its molecular structure and its acid anhydride moiety, NCA is highly electrophilic such that its ring-opening reaction can be induced not only by strong bases such as alkyllithium but also by weak bases such as amines, alcohols and water. The most frequently used initiators are amine functions, which react readily with NCA to give rise to the ring-opening reaction (Step 1 in Mechanism A of Scheme 2.4). As the resulting carbamic acid **A** is unstable, carbon dioxide will be immediately released from it to produce the



Scheme 2.4

corresponding amine **B** (Step 2). The amine then reacts with another NCA molecule to allow a chain growth of polypeptides. Besides this conventional anionic mechanism (Mechanism A), an activated monomer mechanism (Mechanism B) is also possible for the polymerization of NCA. NCA has an acidic N–H proton, which can easily be abstracted under basic conditions. The resulting ionized NCA is sufficiently nucleophilic so as to attack another NCA molecule to form an amide anion **C** (Step 1 in Mechanism B), which will act as a base to abstract the N–H proton of another NCA molecule (Step 2). As a result, N-acylated NCA **D** and ionized NCA are formed, and their reaction allows the chain extension of the polypeptide.

2.3

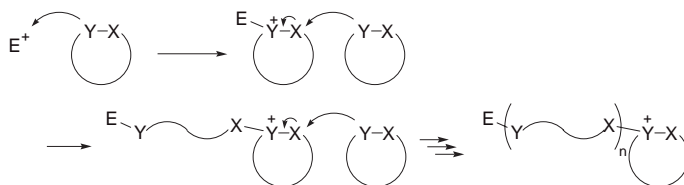
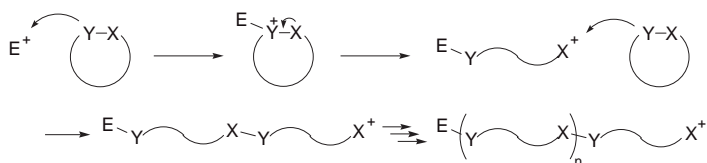
Cationic Ring-Opening Polymerization

2.3.1

General Mechanism

In contrast to anionic ROP, ‘cationic ROP’ represents another class of polymerization where ‘electrophilic’ reagents are used as initiators. A general mechanism for cationic ROP is described in Scheme 2.5, where the initiators with an electrophilic nature most often involve Brønsted acid, Lewis acid and alkyl esters of strong organic acids such as sulfonic acid.

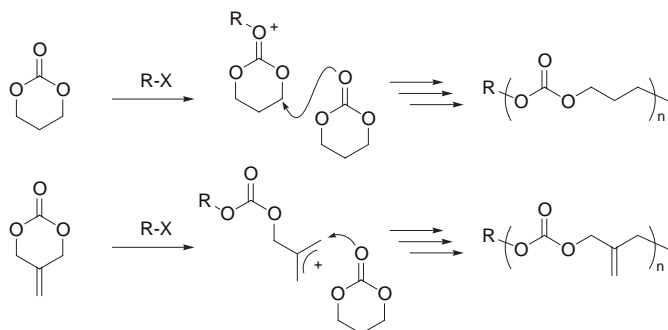
Similar to the monomers capable of anionic ROP, those able to undergo cationic ROP have polarized bonds represented by Y–X, where Y (atom or functional group) has a lone electron pair so that it can act as Lewis base to react with

S_N2 Mechanism**S_N1 Mechanism****Scheme 2.5**

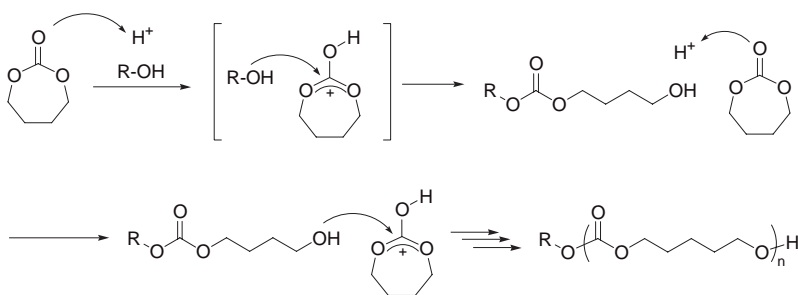
electrophiles. X, which will become a cationic center as a result of the ring-opening reaction, should be an atom in an electron-rich situation, such as an alkoxy-substituted carbon atom. In this way the ring-opening reaction of the monomer will be triggered by a nucleophilic attack of Y towards the electrophilic initiator (represented by E^+). The resulting cationic species, which have a cyclic structure, can be attacked by Y in another molecule of the monomer to undergo a ring-opening reaction (S_N2 mechanism); alternatively, they can undergo a ring-opening reaction spontaneously to produce an acyclic cationic species that will be attacked by the monomer (S_N1 mechanism). The degree of predominance of one of these two mechanisms over the other one depends on the stability of the X^+ cation. When X^+ is sufficiently stabilized by some factors such as electron donation by its neighboring atoms and functional groups, its lifetime will be increased such that the S_N1 mechanism will be predominant. For example, a six-membered cyclic carbonate without substituents undergoes ROP via a S_N2 mechanism [9], whereas a similar cyclic carbonate having an *exo*-methylene group undergoes ROP via a S_N1 mechanism due to the formation of allyl cations stabilized by electronic delocalization (Scheme 2.6) [10].

2.3.2**Activated Monomer Mechanism**

An activated monomer mechanism may also be found in some cationic ROP reactions. In these cases, the cationic species is not the chain end of the polymer, but rather the 'activated monomer'. For example, a seven-membered cyclic carbonate undergoes polymerization in the presence of alcohol and Brønsted acid as the initiator and activator, respectively [11]. The first step consists of protonation of the carbonyl oxygen of the monomer to produce the activated species, which reacts readily with the alcohol. The corresponding ring-opening reaction produces an acyclic carbonate having a hydroxyl group, of which reaction with another



Scheme 2.6



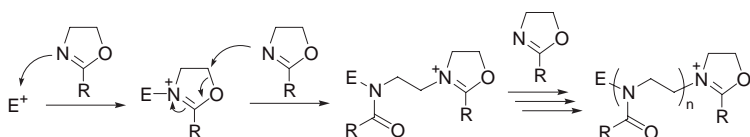
Scheme 2.7

molecule of the activated cyclic carbonated allows chain extension. The resulting polycarbonate has an R residue which is derived from the initiator alcohol and a hydroxyl group at the chain ends (Scheme 2.7).

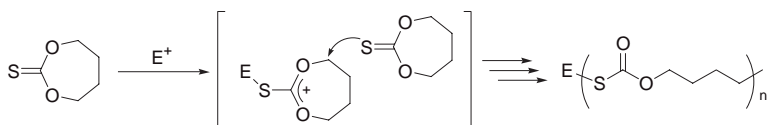
2.3.3

Isomerization Polymerization

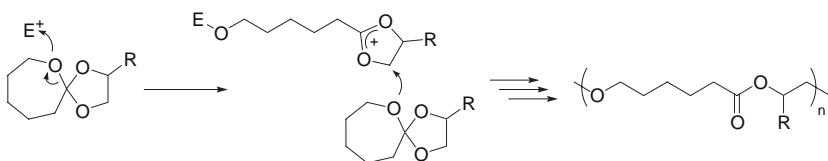
As can be seen from the general mechanism in Scheme 2.5, the ring-opening reaction accompanies cleavage of the functional linkage (X–Y) to form the cationic species in the chain end. This propagating chain end reacts with the monomer to form the X–Y chemical bond again. In other words, the X–Y bond in the monomer will be quantitatively incorporated into the corresponding polymer. On the other hand, there are many examples in which the X–Y bond is not directly inherited by the polymer; rather, the functional group in the monomer isomerizes into another form, which is thermodynamically more stable. Such isomerization–polymerizations proceed smoothly by using the isomerization process as a driving force, and are free from back-biting reactions. Typical examples are shown in Schemes 2.8 and 2.9. The former example is the cationic ROP of oxazoline [12–14]; here, the Lewis basic nitrogen atom in oxazoline attacks an electrophilic initiator to form the corresponding imminium cation, which is then attacked by oxazoline



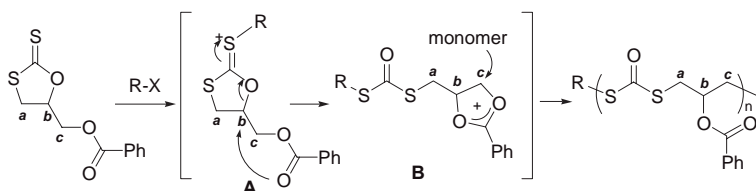
Scheme 2.8



Scheme 2.9



Scheme 2.10



Scheme 2.11

to undergo a ring-opening reaction. The ring-opening reaction accompanies the isomerization of an imino ester in the monomer into an amide in the side chain of the formed polymer. The latter is an example of the cationic ROP of cyclic thiocarbonate, which proceeds with the isomerization of $-\text{O}-(\text{C}=\text{S})-\text{O}-$ into thermodynamically more stable $-\text{S}-(\text{C}=\text{O})-\text{O}-$ [15].

Having such a deep insight into various isomerization processes allows the design of unique monomers and the corresponding cationic ROP. Such an example is shown in Scheme 2.10, which represents the double ring-opening polymerization of a spiro-orthoester [16]. The resulting polymer is a linear polyester, of which the structure seems far away from that expected from the monomer structure; however, by considering the stepwise ring-opening reactions of the two cyclic structures in the monomer and the isomerization process in the latter ring-opening reaction, its formation can be reasonably explained.

The next example involving an isomerization process is the cationic ROP of five-membered cyclic dithiocarbonate (Scheme 2.11) [17]. Upon the addition of RX

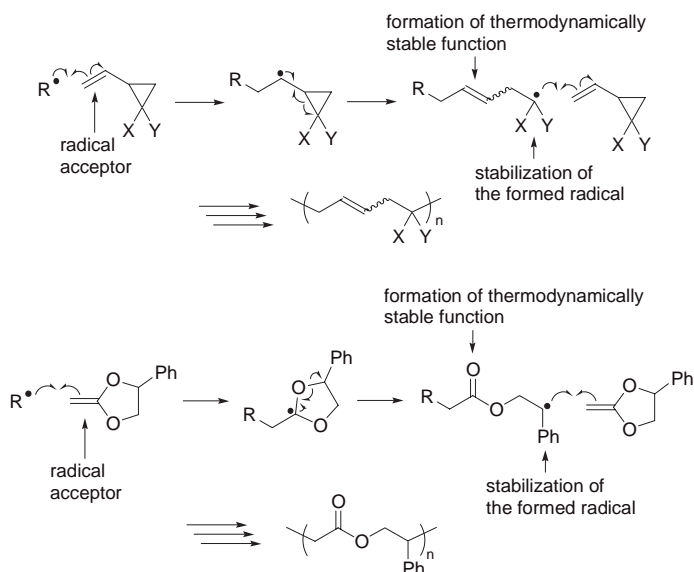
(typically, alkyl trifluoromethanesulfonate) to the monomer, the sulfur atom is alkylated to form a cationic species **A**. In the monomer, an ester group is located such that its carbonyl oxygen can attack the dithiocarbonate ring intramolecularly. This neighboring group participation results in the formation of a new cationic species **B**, to which the monomer molecules react successively to yield the corresponding polymer. The --S--(C=S)--O-- structure in the monomer is isomerized into the thermodynamically more stable --S--(C=O)--S-- structure in the polymer, and this isomerization serves as the driving force to promote polymerization. In addition, the oxonium cation in species **B** is stable enough for its presence to be confirmed by nuclear magnetic resonance (NMR) spectroscopy. In fact, this high stability of **B** allows the polymerization to proceed in a ‘living’ fashion—that is, in the absence of termination and transfer reactions. Due to the neighboring group participation and the resultant isomerization, the methylene group ‘*c*’, which is located outside the dithiocarbonate ring, is incorporated into the main chain of the polymer (see Scheme 2.11).

2.4

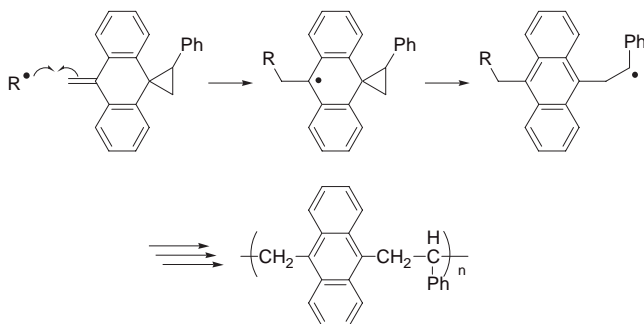
Radical Ring-Opening Polymerization

In this final section we describe free-radically induced ROP [18]. As seen for the mechanisms of anionic and cationic ROP, the indispensable requirement for monomers in ionic ROP is that they possess highly polarized functional groups in order to undergo ‘heterolytic’ dissociation. However, this requirement is not essential for free-radically polymerizable monomers, where the cyclic structure undergoes ‘homolytic’ dissociation. Two typical examples of successful monomer designs are shown in Scheme 2.12. The first (upper) example is the radical ROP of vinyl cyclopropane [19]; here, the vinyl group accepts a radical, while a newly formed radical will be transformed into a carbon radical stabilized by the X and Y substituents, which can be chosen from halogen, aromatic and ester groups. This stabilization effect, as well as the formation of an internal olefin, assists the smooth ring-opening reaction of the cyclopropane ring. The second (lower) example shown in Scheme 2.12 is the free-radical ROP of a ketene acetal, in which the *exo*-methylene group acts as a radical acceptor. Here, the ring structure will undergo a ring-opening reaction with formation of a thermodynamically stable ester bond and a radical which is stabilized by the phenyl group [20].

This radical ROP is considered as a useful tool for synthesizing various polymers having functional groups that cannot be produced by the chain polymerization of vinyl monomers. In addition, recent advances in ‘living’/controlled radical polymerization techniques have provided opportunities of controlling radical ROPs, leading to polymer chains having predictable molecular weights [21]. As an example, the method of radical addition fragmentation transfer (RAFT), which provides one of the most reliable and versatile means of controlling radical polymerizations, has been applied to the radical ROP of a cyclopropane derivative



Scheme 2.12



Scheme 2.13

(Scheme 2.13) [22]. In this case, the process of aromatization to yield an anthracene moiety is the predominant driving force that promotes the polymerization, by which the corresponding anthracene-bearing polymer with a precisely controlled molecular weight can be obtained. One feature of radical ROP that has attracted much attention from polymer chemists is the potential to undergo radical copolymerization with conventional vinyl monomers such as styrenics, acrylics and methacrylics. Recently, a controlled radical copolymerization of methyl methacrylate and a cyclic monomer has been reported [23]. By using a copolymerization, a ketoester linkage can be incorporated into the main chain such that the copolymer produced may be both hydrolyzable and photodegradable.

2.5

Summary and Prospects

In this chapter, we have discussed the fundamental mechanisms for anionic, cationic and radical ROPs by outlining some specific examples that simplify our understanding of these reaction mechanisms. Today, ROP is regarded as an indispensable method for synthesizing polymers with heteroatoms in the main chain, and is also used to complement the chain polymerizations of vinyl monomers. A range of 'living'/controlled ROPs has been developed by which the construction of well-defined polymer architectures exhibiting unique properties has been achieved.

A correct understanding of the mechanisms, based on fundamental organic chemistry, is essential not only when applying ROPs in the production of materials with desired performances and functions, but also when designing new monomers, initiators, catalysts and polymerization media, all of which will surely afford unprecedented polymeric materials to support future industries. In this regard, recent major advances in the analytical techniques used to characterize macromolecules—including MALDI-ToF mass spectrometry and multi-dimensional NMR—have had a major impact on polymer chemists. Moreover, the same techniques will allow the discovery of new reaction pathways previously dominated by other reactions, and in turn lead to development of sophisticated means by which ROP can be controlled in precise fashion. Some key examples of these techniques are provided in later chapters of this book.

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3

Siloxane-Containing Polymers

François Ganachaud and Sylvie Boileau

3.1

Introduction

Polysiloxanes, which have chains constructed from alternately arranged silicon and oxygen atoms with organic groups attached to the silicon atoms, possess a large variety of structures, each differing in their topology and the constitution of their organic substituents. Many and various types of siloxane copolymers also exist. The constantly expanding production and applications of polysiloxanes—and, in particular, their growing use in the elaboration of various well-defined macromolecular architectures—require a detailed knowledge of the reactions used in their synthesis. The ring-opening polymerization (ROP) of cyclic oligomers is the primary route to the majority of silicon polymers and copolymers. This allows the synthesis of high-molecular-weight polysiloxanes with a better precision than the polycondensation process of functional precursors (see the rich review literature already published on this topic [1–14]). The main academic and industrial current problems are, surprisingly, the same as have been raised for at least the past 40 years, namely: (i) a better control of the ROP process in order to depress significantly the back-biting reactions that generate undesirable small cycles that must be removed from the material before use; and (ii) an optimized process to obtain perfectly mono- or difunctionalized polysiloxanes having an index of polydispersity which is as low as possible, that can be used as precursors for more complex architectures such as block and graft copolymers, networks and dendrimers.

In this chapter we consider the two general methods of ROP of cyclosiloxanes: (i) the equilibrium polymerization, which is commonly used when the polymer yield at equilibrium is relatively high; and (ii) the non-equilibrium polymerization, which is quenched before equilibrium is attained. Moreover, both anionic and cationic processes—the mechanisms of which are quite complex—can be used for the ROP of cyclosiloxanes, and are treated independently here. A special emphasis is placed on both cationic and anionic polymerizations of cyclosiloxanes in aqueous media throughout the chapter, as this represents an original and sustainable

process for the preparation of silicone polymers (for a recent review, see Ref. [15]).

Among the many siloxane monomers, the two most important are octamethylcyclotetrasiloxane (D_4) and hexamethylcyclotrisiloxane (D_3), the polymerization of which will be described first. Other numerous cyclosiloxanes are also available by (possibly partial) substitution on the silicon atom of various organic radicals (vinyl, phenyl, trifluoropropyl, etc.) which give rise to functional silicone polymers. Cyclic monomers which contain other groups in addition to siloxane in their skeleton (such as carbosiloxanes), are also considered, which undergo polymerization via the breaking of a siloxane bond. For the sake of brevity, we have purposely avoided any discussion of ROPs of cyclic silanes, silazanes or metal-containing, silicon-based cycles, which do not involve a siloxane bond opening, and for details of these the reader is directed elsewhere [16–19]. Although several references relating to polydimethylsiloxane (PDMS)/organic block copolymers are cited throughout the chapter, these are not treated as a separate entity within the chapter.

Some general details related to the synthesis of PDMS are first presented (independent of publication date), followed by details of more recent fundamental studies that were conducted within the past decade but not included in two recent reviews [13,14].

3.2

Polydimethylsiloxanes

3.2.1

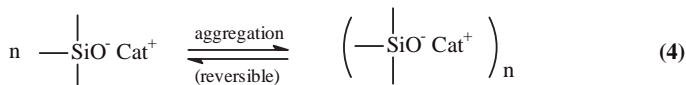
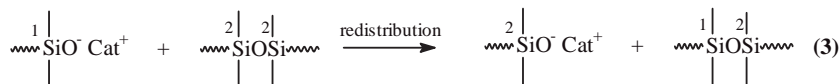
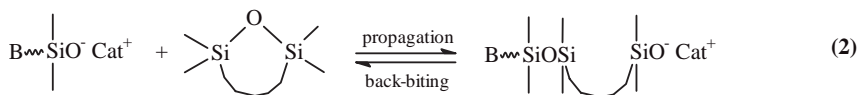
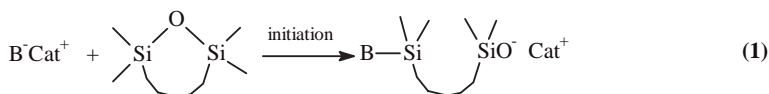
Anionic Polymerization

3.2.1.1 General Considerations

Initiation of the ROP of cyclosiloxanes by bases leads to formation of the silanolate anion (Scheme 3.1; Equation 1); this is the active propagation center, and is capable of extending the polysiloxane chain by the addition of monomers (Equation 2). Here, Cat^+ is usually an alkali metal, quaternary ammonium or phosphonium cation [13], with numerous initiators having been used for the ROP of D_3 and D_4 (most are listed in Ref. [14]).

The propagation step is reversible due to a back-biting reaction of the active center with its own chain, and this leads to the formation of a series of cyclic monomers of various ring sizes. The silanolate may attack a Si–O bond of another chain, leading to the chain transfer (Equation 3), and this results in chain randomization. In the absence of any protonic impurities, the reaction proceeds without termination, while the polymerization can be quenched to deactivate the silanolate center.

The overall rate of polymerization, as well as the relative rates of the component reactions, depend on the initiator, medium and monomer. The nature of the active centers is a key factor when interpreting kinetic data. In most systems, the free silanolate anions do not appear in any kinetically significant concentrations, and



Scheme 3.1

consequently the ion pairs serve as the active propagation species. These are in equilibrium with aggregated species, which are inactive. This aggregation greatly reduces the polymerization rate, and this in turn is responsible for the fractional order of polymerization with respect to silanolate concentration. For example, in the case of $\sim\text{Me}_2\text{SiOK}$ in bulk PDMS and $\sim\text{Me}_2\text{SiOLi}$ in tetrahydrofuran (THF), n equals 2 [11] and 3 (4 if $[\text{SiOLi}] > 10^{-2} \text{ mol l}^{-1}$) [20], respectively (see Scheme 3.1; Equation 4).

The rate of polymerization is directly related to the size of the counterion, and increases strongly in the series: $\text{Li}^+ < \text{Na}^+ < \text{K}^+ < \text{Rb}^+ < \text{Cs}^+ \sim \text{Et}_4\text{N}^+ \sim \text{Et}_4\text{P}^+$ [11]. The rate also increases on adding activators such as hexamethylphosphorous triamide (HMPT), dimethylsulfoxide (DMSO), dimethylformamide (DMF), *N*-methylpyrrolidone (NMP), all of which reduce the ion-ion interaction and decrease the amount of aggregates formed [13, 21–25]. Aggregation was completely suppressed when the lithium cation was complexed by the [2,1,1] cryptand [26–30]. In this last case, only one type of active species was identified (namely cryptated ion-pairs), which are very reactive, and a first order in silanolates was observed. Due to the simplicity of the system, propagation rate constants as well as rate constants for larger ring formation (back-biting reactions) have been determined for D_3 , D_4 , D_5 and D_6 . The order of reactivity of D_x is as follows: $\text{D}_3 \gg \text{D}_4 > \text{D}_5 > \text{D}_6$. Cyclotrisiloxanes show a particularly high reactivity, due to their having the largest ring strain and planar conformation [31]. However, a significant increase in reactivity towards the alkali metal silanolate centers has been observed in a series of unstrained cyclodimethylsiloxanes: $\text{D}_4 < \text{D}_5 < \text{D}_6 < \text{D}_7 < \text{D}_8$, when the reaction was performed in the bulk, or in a nonpolar solvent [13, 32]; such an effect could be explained by a multidentate interaction of siloxane with the counterion. The formation of crown ether-type complexes between Li^+ and K^+ with D_6 and D_7 , respectively, could explain the unexpected enhanced reactivity of those monomers compared to D_4 [33]. The reverse order of reactivity of D_x is observed when

interaction between the alkali counterion and the SiO groups is suppressed—that is, by using polar additives, crown ethers or cryptands or bulky counterions (see below).

3.2.1.2 Recent Advances

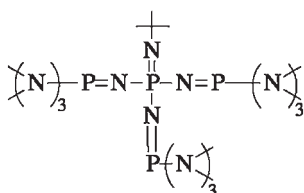
The nonequilibrium anionic ROP of cyclosiloxanes exploits the reactive ring-strained cyclotrisiloxanes as monomers, and this allows the polymerization to be performed with minimal back-biting and chain randomization. The polymerization must be quenched soon after a high monomer conversion is obtained, in order to reduce the re-equilibration reactions that occur during the second stage of the process [13, 34]. In this particular issue, MALDI-ToF mass spectrometry has served as an important tool when studying the mechanism of polymerization of D_3 initiated by *sec*-BuLi [35] and *n*-BuLi [36], in THF. The technique also provides an accurate assessment of the polymer end-groups [35].

The choice of a specific initiator or initiator/solvent system to eliminate the redistribution reactions is crucial, and several means of achieving this have been explored:

- As noted above, systems containing basic additives that interact more strongly with counterions, such as HMPT, DMSO, DMF and NMP [13, 21–25].
- Polymerization can be carried out in a basic solvent, using a hard counterion which interacts with solvent more strongly than with SiO bonds; an example is Li^+/THF . Side reactions have been avoided when carrying out the ROP of D_3 first at room temperature to about 50% conversion, and then at $-20^\circ C$ until complete conversion. The PDMS produced show a narrow molecular weight distribution ($M_w/M_n \sim 1.1$), and are not contaminated by any additives [37].
- In addition to cryptates [26–30] or crown ether complexes [32] (as noted above), bulky and soft, weakly interacting counterions, such as Me_4N^+ , Bu_4P^+ , rare earth complexes [38] and phosphazanium cations [39–45] have also recently been studied.

In particular, nonionic phosphazene ‘superbases’ are extremely effective initiators for the ROP of cyclosiloxanes. An interaction with a proton donor such as methanol, leads to the formation of a silanolate with a very bulky phosphazanium cation, having a delocalized positive charge. This $t\text{-BuP}_4\text{Me}_{18}$ (see structure below), at a concentration of $10^{-3} \text{ mol l}^{-1}$ and with an equivalent of MeOH at room temperature, induces almost instantaneous polymerization of D_4 [39, 40]. The imino-oligophosphazene bases also serve as very active promoters when used with alkali metal initiators of the ROP of cyclosiloxanes [39]. Within the same family, other initiators used are amino-substituted oligophosphazanium hydroxides, such as $[(R_2N)_3PNP(NR_2)_3]^+ OH^-$, where R is a pyrrolidine group, which do not require any coactivation. These are also highly efficient initiators for the ROP of D_3 and D_4 [42, 45], with reactions (in toluene) being first order both in monomer and in initiator. The activation energy, as well as the activation entropy values for D_3 , are almost the same as in the case of Li^+ [2,1,1] (11 kcal mol^{-1} and $-21 \text{ cal mol}^{-1} K^{-1}$

compared to $9.8 \text{ kcal mol}^{-1}$ and $-20 \text{ cal mol}^{-1} \text{ K}^{-1}$ [27]). The rate constant of propagation was seen to be higher with this system than with lithium cryptate as counterion. Further detailed studies on the nature of the active centers would be valuable when interpreting the kinetics of this very promising system. Less expensive initiators have also been examined, including a novel system combining an alcohol and a phosphorus ylide [46], as well as N-heterocyclic carbenes [47], both of which are efficient for the ROP of D_4 , under mild conditions.



t-BuP₄Me₁₈

End-functionalized polysiloxanes are prepared by using a nonequilibrium ROP of cyclosiloxanes, as this allows a good control of the molecular weight, molecular weight distribution and functionalization. Functionalization of the chain-ends is achieved by using either a functional terminating agent or a functional initiator [13]. The latter strategy offers several advantages over conventional electrophilic termination reagents, because each functionalized initiator molecule produces a macromolecule with the desired functionality, regardless of the molar mass of the polymer. In this way, any problems associated with terminating agents, such as their efficiency and selective reactivity, and the stability of the anionic chain-ends, are avoided. Thus, 3-[(N-benzyl-N-methyl)amino]-1-propyllithium [48], as well as lithioalkoxyamines [49–52], have been used as initiators of the ROP of D_3 to give PDMS with a terminal secondary amine in the first case, whereas the second type of initiator led to the synthesis of block copolymers by controlled radical polymerization. Oligodimethylsiloxanes containing a 2-pyrrolidone moiety at one chain-end have been obtained by ROP of D_3 initiated by lithium (1-alkyl-2-pyrrolidon-3-yl methyl)dimethyl silanolate [53]. According to the same strategy, heterotelechelic PDMS has been prepared by using lithium methacryloxypropyldimethylsilanolate as the initiator; this has also been used as a precursor for the synthesis of PDMS-*b*-polyethylene oxide (PEO) diblock copolymers [54]. The anionic nonequilibrium ROP of D_4 , when initiated by silazyl-lithiums, produced a narrow molecular weight PDMS ($M_w/M_n \sim 1.3$) with silanamine end-groups [55].

Finally, it should be noted that D_3 and D_4 were anionically polymerized in heterogeneous systems, using trimethyl benzyl ammonium resins covered with OH^- catalyst, in either the absence [56] or presence [57] of a chain-end terminating agent. In the former case, rapid polymerization reactions at moderate temperature resulted in moderate yields (generally less than 50 wt%) of silicones of limited molar masses (typically around $20\,000 \text{ g mol}^{-1}$), due to the presence of residual water in the system inducing back-biting reactions. By introducing bis(aminopropyl-tetramethyldisiloxane), however, telechelic functional polysiloxanes were obtained,

although again the experimental degree of polymerization (DP) was far from that expected (based on theory) for a 100% introduction of dimethyldisiloxane units, and with a lesser efficiency than in an acid-catalyzed heterogeneous polymerization (see below).

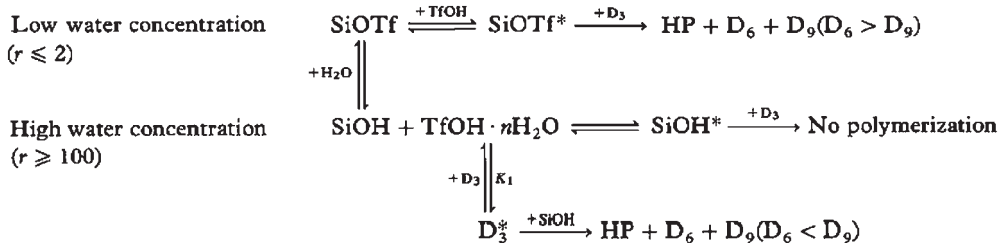
3.2.2

Cationic Polymerization

3.2.2.1 General Considerations

A review published in *Comprehensive Polymer Science* on the ROP of cyclosiloxanes [3] detailed the main results accumulated for the cationic polymerization of cyclosiloxanes during the past 50 years. Here, the issues of the polymerization of cyclosiloxanes in solution, using a superacid (triflic acid) as the catalyst will be summarized. The main results were first reported by Chojnowski and colleagues [58–63], and subsequently by Sigwalt and coworkers [64–66], with both groups generally agreeing on the main features of the mechanism of polymerization in dichloromethane (DCM). Under strictly anhydrous conditions, the ring-opening reaction of D_x (typically $x = 3$ or 4) with triflic acid (TfOH) produces a silyl triflate ester silanol, $HO[Si(CH_3)_2O]_xTf$, which immediately leads to the diester molecule, either by coupling or (more likely) by esterification. The released water forms different adducts with the triflic acid, $TfOH \cdot (H_2O)_r$, where $r = 1$ or 2 (upper equation, Scheme 3.2). The monohydrate $H_3O^+ \cdot TfO^-$ then activates the ester function (which is inactive *per se*), leading to chain propagation either directly on the activated ester or on a transitory siloxonium ion. The rate of polymerization and products formed are quite different whether D_4 or D_3 polymerizations are studied. The polymerization of unstrained D_4 is slow, with competing polymerization and depolymerization reactions which lead first to the formation of larger cycles D_5 , D_6 and D_7 , in decreasing concentrations. The high polymer is generated only after an induction period, with the uncontrolled molar masses arising both from a chain reaction involving activated silyl triflates and also possibly from condensation between triflates and silanols [67, 68]. On completion of the polymerization, the equilibrium between the high polymer and cycles is established with $[D_4] > [D_5] > [D_6] > [D_7] \dots$

The polymerization of D_3 in DCM with TfOH is rapid and controlled kinetically, with a linear increase in molar mass with conversion from the origin and corresponding to a theoretical M_n , as in a living system. However, there occurs a simultaneous and proportional formation of some macrocycles, together with very



Scheme 3.2

large amounts of D_{3x} cycles, with D_6 , D_9 and D_{12} in decreasing proportions. In fact, the amount of D_6 sometimes approach that of the high polymer. This prominent D_{3x} cycle formation was tentatively explained by a specific back-biting reaction of $\text{Si}-\text{D}_3^+$ transitory oxonium end-groups, involving the formation of a strainless eight-membered oxonium transition state [66], rather than an end-closure reaction of a short oligomer functionalized by a silanol and a silyl triflate ester groups. Indeed, by introducing a monofunctional initiator—namely $\text{PhCH}_2(\text{CH}_3)_2\text{SiOTf}$ —Sigwalt and coworkers observed a major decrease in the formation of macrocycles, whereas the proportions of D_6 (and, to a lesser extent, of D_9) did not change [69].

In the presence of a large excess of added water compared to triflic acid (see Scheme 3.2, lower equations) [70], the silyl esters are progressively hydrolyzed into silanol groups, and may eventually disappear when $r \geq 100$. Under these conditions, large molar mass polymers (including macrocycles) and D_{3x} cycles are formed in very different proportions, showing that D_3 polymerization (presumably through an activated monomer mechanism) and condensation reactions (including end-closure) actually compete one with another.

3.2.2.2 Recent Advances

Triflic acid was also used to better apprehend the polymerization mechanism of less strained cycles. A study on the solution polymerization of cyclosiloxanes with increasing ring size (from three to seven units) showed that, whereas the much faster D_3 polymerization rate could be ascribed to the ring strain in this near-planar structure, the propagation rate constants of larger cycles were increased with ring size ($D_4 < D_5 < D_6 < D_7$), this being a consequence of their increasing flexibility [71]. When short siloxanediols are added to D_4 [70] or D_3 [72] in their solution polymerization (e.g. in DCM at 30 °C), initially only the polycondensation of silanols is observed, without any polymerization of the cyclic monomers. However, when the silanol concentration becomes sufficiently low, a conventional ROP of D_3 takes place (see Scheme 3.2, lower equations), whereas no polymerization occurs with D_4 . A mixed anhydride of trifluoroacetic acid (TFA) and triflic acid allowed a significant suppression of the release of water previously seen in the triflic acid system. Under certain conditions, although the macrocycle content may be zero, D_6 is still formed in large proportions. [73].

As stated earlier by Chojnowski and Cypryk [13], a functional disiloxane can also be introduced in the DCM, in addition to triflic acid, to generate α,ω -telechelic PDMS for use in further grafting reactions, such as divinyltetramethyldisiloxane V_2 [74] or tetramethyldisiloxane M_2^H [75]. Another team also functionalized polystyrene chains (prepared by radical polymerization) on both ends with pentamethyldisiloxane groups to produce, through triflic acid redistribution with D_4 , a triblock copolymer; this technique was quoted by the authors to be easier than the conventional approach, which employs the sequential anionic polymerization of both monomers [76]. Another example worthy of mention here is that reported by Cai and Weber, who started with a tetrakis Si–H-functionalized precursor (tetrakis (dimethylsiloxy)silane) to generate silicone stars [77].

Today, several research investigations have been devoted to the quest for new, efficient initiators that could replace triflic acid. An even more superacidic catalyst,

namely bis(trifluoromethane) sulfonimide, increased the polymerization rate of D_4/M_2 system, while retaining the other features of the process (large yields, efficient chain-termination) [78]. In most cases however, the use of a tailored initiator/catalyst complex which limits the content of acidic catalyst in the medium, is preferred. Jallouli and Saam proposed the polymerization of ring-strained cyclosiloxanes (including D_3) by trimethylsilyltriflate, and used a proton trap (2,6-di-*t*-butylpyridine) to tentatively remove all traces of residual triflic acid resulting from hydrolysis [79]. The long induction period, which was found to depend on the content of the proton trap, led the authors to suspect that an intermediate pyridinium triflate could in fact activate the triflate initiator, in place of the triflic acid that was previously required for the polymerization to proceed [69]. Olah *et al.* [80], by reacting siloxanes in DCM at -70°C with a silane and $\text{Ph}_3\text{C}^+\text{B}(\text{C}_6\text{F}_5)_4^-$, demonstrated the presence of long-lived siloxonium cations (e.g. MeSiD_3^+ with D_3), which could no longer be traced above -30°C . Nonetheless, the polymerization of D_3 and D_4 proceeded at 0°C . Although the propagation was assumed to occur via siloxonium ions, it may also have involved silanol end-groups reacting with $\text{H}^+\text{B}(\text{C}_6\text{F}_5)_4^-$, since very little D_6 was formed in the polymerization of D_3 . Subsequently, Chojnowski *et al.* polymerized D_3 in toluene initiated by $\text{H}^+(\text{H}_2\text{O})\text{B}(\text{C}_6\text{F}_5)_4^-$ [81]. An interesting report from Olah and coworkers described the synthesis of triblock copolymers, starting from telechelic polystyrene with Si–H end-groups, and of hypergrafted all-silicone polymers which were created by growing PDMS branches onto a polymethylhydrosiloxane (PMHS) backbone [80]. Moreau, Sigwalt and colleagues [82] used HCl as an initiator and SbCl_5 as a coinitiator at -10°C ; when the M_n was controlled via the HCl concentration, very little D_6 (much less than D_5) and no macrocycles, were formed. This ability to control the polymerization was explained by the propagation involving silanol end-groups and D_3 activated by $\text{H}^+\text{SbCl}_6^-$. Although phosphoronitrile halides were tested as a non-ionic Lewis acid catalyst, it was shown later that hydrolysis of this catalyst caused the release of HCl, which was the true initiator of polymerization [83]. Very recently, the team of Chojnowski used the $\text{R}_3\text{SiH}/\text{B}(\text{C}_6\text{F}_5)_3$ system to promote the polymerization of D_3 in solution and generate tailored oligomer structures with Si–H end-groups or larger molar mass polymers [84].

The heterogeneous polymerization/redistribution of D_4 and a bifunctional disiloxane, using strong acid resins or clays, to generate telechelic PDMS with various functionalities, has long been practiced and, indeed, continues to be used in industry. The heterogeneous polymerization of cyclosiloxanes mainly uses sulfonic acid resins or acidified clays in the monomer bulk, with the major benefits of the process being the easy filtration of the catalyst after reaction, and the stability of the thus-prepared polymers. Two groups [85, 86] carried out the D_3 and D_4 ROP in the absence of a terminating agent, the aim being to ‘control’ the molar masses by tailoring the content of water in the medium (though this requires very careful experimentation). However, the majority of the studies, mainly from the group of Govedarica [87–90], reported using a functional M_2 -type molecule as chain-controller, thereby introducing different functionalities (e.g. vinyl, carboxylic, hydroxyl) at the chain-ends. The details of various studies are listed in Table 3.1,

Table 3.1 Cationic heterogeneous homopolymerization of cyclosiloxanes.

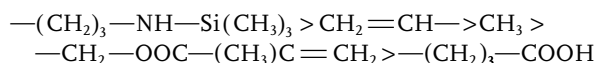
R of functional molecule ^a	Cycle	Catalyst ^b	Conversion (%)	M_n (kg mol ⁻¹)	M_w/M_n	Reference
CH ₃ , CH=CH ₂ , (CH ₂) ₃ COOH	D ₄	SR	~90	10–43	–	[87]
CH=CH ₂ , (CH ₂) ₃ NHSi(CH ₃) ₃ , (CH ₂) ₃ -acrylate, (CH ₂) ₃ COOH	D ₄	SR	80–90	0.8–1.2	1.4–1.9	[57]
H	D ₄	AC	80	8	1.9	[88]
H, CH ₃ , CH=CH ₂ , (CH ₂) ₃ COOH	D ₄	SR	–	–	–	[89]
(CH ₂) ₃ COOH	D ₄	SR	88–95	0.6–3.5	1.2–1.6	[90]
CH ₃ ^c	D ₃ , D ₄ , D ₅	SR	–	0.75–2.4	–	[91]
CH ₃	D ₃ , D ₄	SR	–	–	–	[92]
(CH ₂) ₃ OCH ₂ CH(OH)CH ₂ OH	D ₄	AC	–	15–32	–	[93]

a The chain-terminating agent has the following structure: R–Si(CH₃)₂–O–Si(CH₃)₂–R, unless stated in the table.

b SR: sulfonic resin; AC: activated clay.

c MD_{8.5}M was also studied here as a terminating agent.

from which it can be seen that, in most cases, the yields were quite good (typically 90 wt% of polymer). The targeted molar masses were generally quite low (below 10 000 g mol⁻¹), whereas the molar mass distribution (MMD) was always less than 2, and often close to 1.5. It should be noted that, although D₃ (as expected) was the most reactive monomer, D₄ was preferred on a cost basis, while D₅ was the least reactive. Chain-terminating agents may also be classified depending on their reactivity, as follows [57]:



3.2.3

Emulsion Polymerization

3.2.3.1 General Considerations

Anionic and cationic homopolymerizations of cyclosiloxanes in stable monomer dispersions, with particle sizes typically less than 1 μm, were first studied extensively in an industrial environment [94, 95], due to their practical interest, inherent reactivity and straightforward preparation. Working in an aqueous medium may have been motivated by the peculiar kinetics (compared to bulk polymerization)

of the many reactions involved in the systems, namely initiation, propagation and reverse back-biting reactions, termination and reverse chain-end reactivation, redistribution, polycondensation and reverse hydrolysis [96]. Miniemulsions, composed of submicronic stable droplets, or microemulsions, with droplet sizes of 20–30 nm, exhibit a sufficiently large specific surface area as to promote interfacial reactions that occur compulsorily in these systems. The small silicone cycles are particularly suited to polymerization in miniemulsions as they are highly hydrophobic, they are not ‘degraded’ at ‘extreme’ pH-values (e.g. pH 2 or 13), but rather polymerize quickly with conventional acid or base initiators, such as protons or hydroxides.

The choice of surfactant is crucial in such a polymerization process, for which all steps (initiation, propagation, termination) are located at the interface (Figure 3.1). The role of the surfactant is to draw the catalyst (H^+ or OH^-) towards the interface and, after initiation, to pair with the propagating chain-ends to generate a bulky, and thus highly reactive, ion-pair. When the chains are generated they grow at a rapid rate until the oxyanion or carbocation undergoes chain transfer to water, which ‘kills’ the chains reversibly. Surfactants bearing ammonium hydroxide and phenyl sulfonic acid heads are preferred when carrying out anionic and cationic polymerizations, respectively. The nature of the alkyl side chains is also important, as it should ensure good stabilization of the monomer droplets after sonication, and limit the content of interfacial water.

In these systems, the final molar mass should only be a function of the ratio of propagation over the termination rate constants, and indeed sometimes will reach several tens of thousands of $g\cdot mol^{-1}$. The fact that propagation generally stops at a relatively low DP, even for living systems (i.e. where termination reaction with water is reversible), has only recently been understood. The so-called ‘critical DP limit’ (see Figure 3.1) corresponds to the point where the deactivated chains are no longer surface-active and prefer to locate in the core of the particle rather than at the interface. Because the chains do not easily return to the particle surface (where they may be reactivated), the propagation simply ceases.

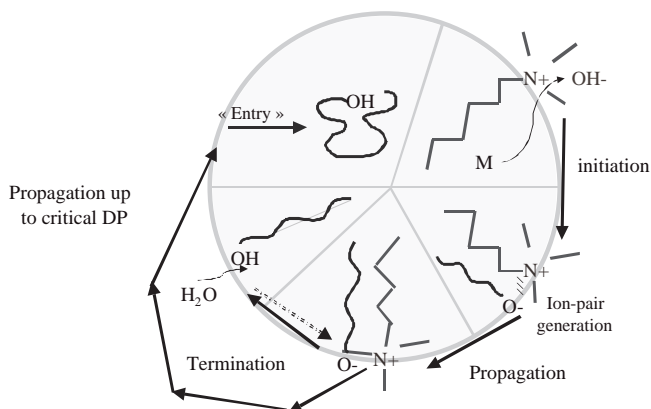


Figure 3.1 Mechanism for interfacial (an)ionic polymerization in a miniemulsion.

3.2.3.2 Recent Advances

Recent studies conducted in academia have highlighted the important future role that sustainable processes may play in the synthesis of silicones. In most studies, similar catalyst/surfactant systems as have been reported earlier were used, principally a fatty sulfonic acid and a quaternary ammonium surfactant [97]. In specific model studies of the anionic polymerizations of D_4 [98], the basic features of ionic miniemulsion polymerization were maintained, including a slow initiation, fast propagation and back-biting, and reversible termination, all of which take place at the interface. Chains were limited to molar masses of about 2500 g mol^{-1} (the critical DP limit for chains propagating on both ends) before increasing after 70% conversion, on the basis of polycondensation reactions. The overall ratio of cycles over linear chains was slightly less than that found for the bulk polymerization thermodynamic equilibrium. Another group which performed an anionic polymerization of D_4 in emulsion, used a mixture of sodium dodecyl benzene sulfonate surfactant and NaOH [99]. Of note, a large surfactant content was required to ensure a satisfactory shelf-life; this was due to the high ionic strength caused by high levels of sodium hydroxide (also, the addition of a small amount of methacryloxytrimethoxysilane (MATS) was required to help polymer crosslinking).

The cationic polymerization of D_4 in a miniemulsion, using dodecylbenzyl sulfonic acid as a catalyst/surfactant, was reported twice at the start of the century, the aim being to prepare core-shell particles (see also Section 3.3.2.2) [99, 100]. Polymerizations at 60–90 °C were relatively slow (taking more than a day), and conversions limited to 85% in the best cases [99], although larger molar masses could be achieved than in the anionic process (typically $183\,000 \text{ g mol}^{-1}$) [100]. Some recent studies [15, 101] have clarified some points of this process. Cycles of various ring sizes are generated initially, before any effective polymerization. The molar masses also increased linearly with conversion; this is in contrast to anionic polymerization, due to a lower water content within the droplets, while D_4 is consumed over the numerous cycle redistribution steps that occur at the start of the polymerization.

Polymerization in very small droplets (typically <30 nm, so-called ‘microemulsions’) was also described recently. Previously, cyclosiloxanes such as D_4 were polymerized using starved-feed microemulsion systems [102], a procedure which inspired numerous patents on the subject. Both, cationic and anionic polymerization processes were shown to be functional, using either a low content of an ionic surfactant, or a mixture of ionic and nonionic surfactants. In this way, particles with diameters as small as 25 nm and with a narrow particle size distribution were produced, and with oil contents up to 40 wt%. Other reports have described the anionic polymerization of D_4 in a microemulsion, using nonionic surfactants and cosurfactants such as ethylene glycol or aminoethanol [103, 104]. Based on the large specific surface area of these 30 nm-sized particles, initiators such as KOH or potassium silanolate could be used with no detrimental effect in polymerization rate. In addition, the instantaneous hydrolysis of dichlorodimethylsilane, in the presence of an electrosteric surfactant (added to resist the high load of ions pro-

duced), first generates cyclosiloxanes that later polymerize according to a conventional cationic polymerization process [105].

Among other original studies, catanionic vesicles were also used as templates for the crosslinking reaction of tetramethylcyclotetrasiloxane or D_4^H inside their bilayers; this led to the creation of nonporous, impermeable, highly crosslinked, water-filled hollow spheres of about 100 nm diameter [106, 107]. Various reports on the preparation of inorganic/organic core-shell particles via a simultaneous or two-step radical and ionic emulsion polymerization are outlined later in the chapter.

3.2.4

Other Processes

When Price *et al.* [108] carried out a solution polymerization of D_4 by employing ultrasound and using sulfuric acid as a necessary catalyst, they reported an enhanced rate of polymerization and a higher average molecular weight (up to $40\,000\text{ g mol}^{-1}$) compared to conventional stirring, while retaining a rather narrow polydispersity (<2). The cationic polymerization of D_4 , using triflic acid, was recently carried out in supercritical CO_2 , for example at 110°C and 150 bar pressure, to achieve significantly enhanced molecular weights (up to $170\,000\text{ g mol}^{-1}$) when compared to regular solution polymerization [109]. In another study, D_3 was first vaporized together with hexafluoropropylene oxide, followed by copolymerization on a hot filament to deposit a highly fluorinated, crosslinked film [110].

Polymerizations on a variety of surfaces, including planar wafers or grounded fillers, have been extensively studied over the past ten years. Different ceramic surfaces were functionalized by silyl triflate moieties to initiate the polymerization of D_3 and to generate a dense, grafted layer of PDMS [111]. The team of Bruzaud described the exfoliation of HTiNbO_5 minerals by the intercalation of PDMS chains, either prepared previously or produced *in situ* [112–114]. The mineral oxide was first activated using an aqueous solution of tetralkylammonium hydroxide, after which the anionic polymerization of D_3 proceeded to generate fully exfoliated nanocomposites (Figure 3.2). Finally, the simultaneous sol–gel chemistry of tetraethoxysilane/tetrachlorosilane, and the ROP of D_3 —both catalyzed by iron oxide—were performed to generate resin-like quantum dots [115].

3.3

Functional Silicones

In recent years, considerable interest has been shown in the functionalization of polysiloxanes with organic side groups to confer special properties to the polymer. Hence, a variety of functional groups have been introduced to organic radicals bound to silicon atoms [116]. The controlled functionalization of polysiloxane side groups may be achieved by the homopolymerization and copolymerization of (preferentially more reactive) cyclotrisiloxanes containing functions in organic substituents. The functionalized polymers of well-defined structure should have a defined molecular weight and low polydispersity, and should exhibit a uniform

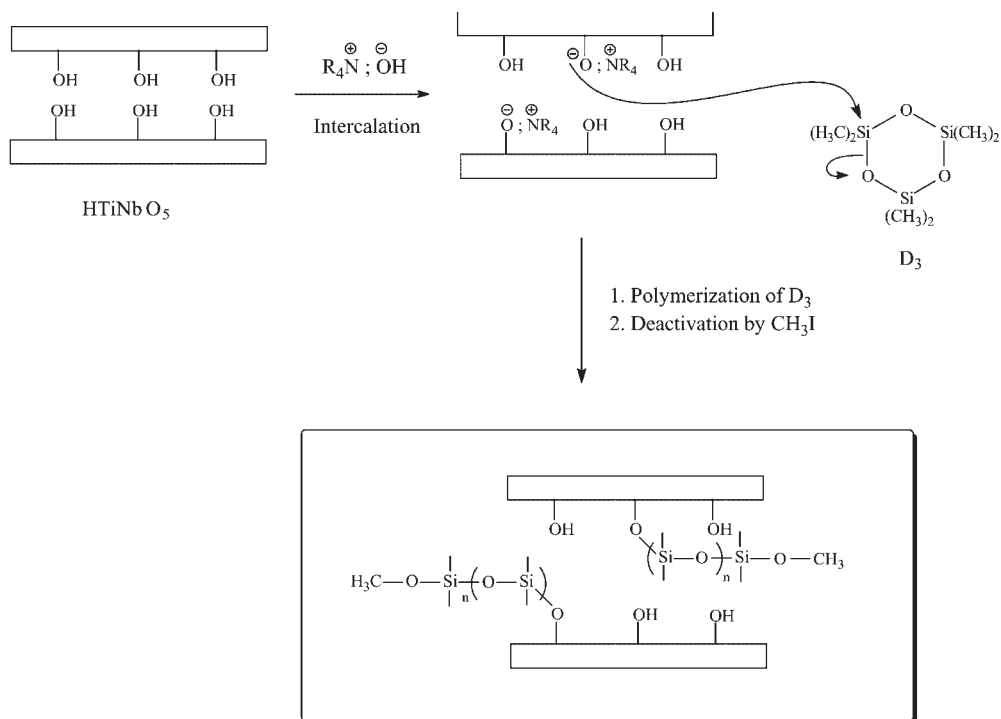


Figure 3.2 Principle of exfoliation of a mineral oxide by an intercalation/polymerization process.

structure of the macromolecules and a well-defined arrangement of functional groups along the chain. This requires conditions in which back-biting and chain-to-chain transfer may be avoided [13]. The polymerization of a monomer with the target functional group is often inconvenient or impossible. Acidic or electrophilic groups do not tolerate anionic propagation centers, and some monomers may be difficult to purify. Thus, the preferred strategy is to use monomers bearing precursor groups, the most common of which are SiH, Si-CH=CH₂ and Si-(CH₂)₃Cl; these are then transformed into target functions within the polymer chains [117].

In the following, two different types of functionalized cyclsiloxanes are described, namely those with functional groups in all siloxane units [(RMeSiO)_n; hereafter referred to as 'symmetrical'], and those partly functionalized [(R₁R₂SiO(Me₂SiO)_{n-1}); hereafter referred to as 'asymmetrical'], where n = 3 or 4.

3.3.1

Anionic Polymerization

3.3.1.1 Homopolymerization of Symmetrical Cyclsiloxanes

The reactivities of cyclotrisiloxanes and cyclotetrasiloxanes differ notably when the methyl groups are replaced by longer alkyl chains, or one or more functional groups are introduced on the cycle. The kinetics of ROP of cyclotrisiloxanes with

Table 3.2 Anionic ROP of symmetrical cyclotrisiloxanes (RMeSiO)₃.

R	Name	Conditions	Comments	Reference(s)
Vinyl	V ₃	Me ₃ SiCH ₂ Li + [2,1,1], toluene, 2 °C	$k_p = 7.21 \text{ mol}^{-1} \text{ s}^{-1}$	[119]
		Ph ₂ Si(OLi) ₂ , THF/HMPA, RT	narrow M_w/M_n distribution	[43] [43]
		P ₄ - <i>t</i> -Bu(superbase), bulk, 80 °C	broad M_w/M_n distribution	[120]
		<i>n</i> -BuLi, THF, 25 °C	<i>cis</i> + <i>trans</i> mixture, low M_w/M_n	
OSiMe ₃	–	Ph ₂ Si(OLi) ₂ , THF/HMPA, RT	<i>cis</i> + <i>trans</i> mixture	[121]
C ₆ H ₅	P ₃	<i>sec</i> -BuLi, cyclohexane, THF, 55 °C	<i>cis</i> isomer, back-biting	[41, 122]
(CH ₂) ₃ Cl	–	BuMe ₂ SiOLi, THF, 25 °C	$[\textit{cis}]/[\textit{trans}] = 1/3.3$, same reactivity of isomers, no side reactions	[123]
(CH ₂) ₂ CF ₃	F ₃	Ph ₂ Si(OLi) ₂ , or Me ₃ SiOLi, Bz or THF, RT	<i>cis</i> isomer, low M_w/M_n	[124, 125]
		Dilithium silanolate, CH ₃ COOEt, 0 °C	<i>trans</i> isomer, low M_w/M_n	[126]
		Polystyryl-Li, THF, 0 °C	<i>trans</i> isomer, low M_w/M_n	[127]
(CH ₂) ₂ C ₄ F ₉	–	KOH, crown ether, 0–20 °C	Poor reproducibility	[128]
		NaOH, 150 °C		[129]

two alkyl chains per silicon atom (C_{*n*}H_{2*n*+1}) have been studied in toluene, by using *sec*-BuLi + [2,1,1] as the initiator. The reactivity of D₃^{Et} and D₃^{Pr} is much lower than that of D₃ ($k_p = 4700, 40$ and $251 \text{ mol}^{-1} \text{ h}^{-1}$ at 20 °C for D₃, D₃^{Et} and D₃^{Pr}, respectively) [30]. From the kinetic data of the ROP of the ‘vinyl’ series (1,3,5-trimethyl-1,3,5-trivinyl-cyclotrisiloxane (V₃) [119], V₄, V₅, V₆ [27], measured in toluene, with *sec*-BuLi + [2,1,1] as the initiator, the reactivity of V₄ and V₅ is almost the same as that of D₃, while that of V₃ is about 20-fold higher than that of D₃. This order of reactivities V₄ ~ D₃ > D₄ also holds for heterogeneous polymerizations catalyzed by ammonium hydroxide resins [56].

In Table 3.2, the cyclic trisiloxanes appear as two isomers, *cis* and *trans*. The microstructure of the polymers bearing trifluoropropyl and phenyl substituents has been reviewed [118]. The rate of polymerization depends to a large extent on the nature of the substituent with, in general, the electron-withdrawing substituents increasing the reactivity, although the situation may be more complex [13].

Some fully functionalized monomers have also been studied recently. Hexa-*n*-alkylcyclotrisiloxanes with side chains ranging from butyl up to decyl have been

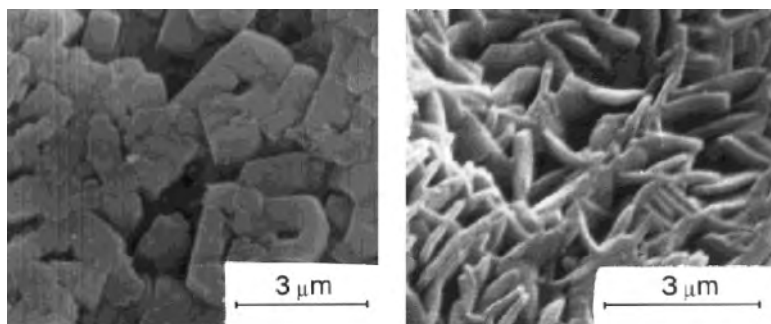


Figure 3.3 Scanning electron microscopy images of polydiphenylsiloxane (PDPhS) samples taken from the reaction mixture of solid-state polymerization of hexaphenylcyclotrisiloxane (HPhTS) under different polymerization conditions. KOH as

the initiator, under an argon atmosphere at 180 °C for 80% conversion of HPhTS (left) and in vacuum at 180 °C for 60% conversion of HPhTS (right). (Images reprocessed from Ref. [131].)

polymerized under the same conditions, but in the bulk, at 60 °C, due to their low reactivity. In this way, polymers with a low polydispersity are obtained, particularly for $n = 4, 5$ and 6 [130]. This was also the case when using the phosphazene base P_2Et as the promoter for the ROP of D_3^{Et} initiated by *sec*-BuLi, in the bulk, at 20 °C [39]. The anionic ROP of hexavinylcyclotrisiloxane, performed using $Ph_2Si(OLi)_2$ as the initiator, and under the same conditions as for V_3 , yields high molecular weight poly(divinylsiloxane) with a narrow M_w/M_n distribution [43]. Solid crystals of hexaphenylcyclotrisiloxane (HPhTS) were polymerized in the solid state by crystalline KOH, deposited on the monomer through an ethanol solution, or potassium oligo-(methylphenylsiloxanolate), a viscous liquid which is easier to spread on the monomer [131]. Although the conditions of polymerization were drastic (typically 180 °C under argon or *in vacuo*), the final polymers showed very large molar masses with, in the best conditions a M_n of about $500\,000\text{ g mol}^{-1}$. The same authors carried out a thorough analysis of the evolution of crystal structure with conversion (see Figure 3.3), and ultimately proposed a mechanism of reaction where polymerization and crystallization of the polymer proceeded successively.

3.3.1.2 Homopolymerization of Asymmetrical Cyclosiloxanes

The polymerization of monomers with mixed units (see Tables 3.3 and 3.4) leads to copolymers of functional siloxane and dimethylsiloxane units.

In each of the listed examples, the propagation is not accompanied by a chain cleavage reaction and the monomer enters the chain undivided; in other words, the distribution of functional units in the macromolecule is uniform (chemoselective reaction) [13]. The order of units may be regular if the propagation occurs regioselectively—that is, if the ring is opened exclusively at one site. The regioselectivity in the ROP of those cycles depends heavily on the nature of the substituent and on the experimental conditions, as can be seen from the data listed in Tables 3.3 and 3.4.

Table 3.3 Anionic ROP of difunctional cyclotrisiloxanes $R_1\text{MeSiO}(\text{Me}_2\text{SiO})_2$.

R_1	Conditions	Regioselectivity (comments)	Reference(s)
H	$\text{Ph}_2\text{Si}(\text{OLi})_2$, THF, -78°C	High	[132]
Vinyl (VD_2)	$\text{Me}_3\text{SiCH}_2\text{Li}$ + [211], toluene, 2°C	Medium ($k_p = 0.55 \text{ l mol}^{-1} \text{ s}^{-1}$)	[119]
	Me_3SiOLi , THF, 0°C	– (Head to tail structure)	[133]
	<i>n</i> -BuLi, THF, -30°C	High	[134]
	Me_3SiOLi , THF, -30°C	High	[117]
$(\text{CH}_2)_2\text{C}_6\text{F}_5$	$\text{Ph}_2\text{Si}(\text{OLi})_2$, THF, 20°C	Poor	[135]
$(\text{CH}_2)_3\text{N-Imidazole}$	$\text{BuMe}_2\text{SiOLi}$, THF, RT	–	[136]
OSiMe_2H	BuLi, THF, HMPA, -25°C	High	[137]
$(\text{CH}_2)_3\text{Cl}$	$\text{BuMe}_2\text{SiOLi}$, THF, 25°C	– (No side reactions)	[123]
$(\text{CH}_2)_2\text{S-}t\text{-Bu}$	$\text{Me}_3\text{SiCH}_2\text{Li}$ + [211], toluene, 2°C	Fair ($k_p = 2.6 \text{ l mol}^{-1} \text{ s}^{-1}$)	[119]
$(\text{CH}_2)_2\text{S-}t\text{-Bu}$	$\text{Me}_3\text{SiCH}_2\text{Li}$ + [221], toluene, 2°C	– ($k_p = 0.22 \text{ l mol}^{-1} \text{ s}^{-1}$)	[119]
$(\text{CH}_2)_2\text{SR}$ (R = <i>iso</i> -propyl, <i>t</i> -butyl, <i>p</i> -methoxybenzyl, naphthyl)	$\text{O}(\text{SiMe}_2\text{OLi})_2$, THF, 25°C	(Slightly more reactive than D_3)	[138]

The ROP of functionalized cyclotetrasiloxanes has been also examined, and some examples are listed in Table 3.5. Here, it is necessary to use highly efficient initiating systems (e.g. lithium cryptates or superbases), as the reactivity of the cyclic tetramers is much lower than that of the corresponding trimers. Copolymers produced in this manner have a less regular structure than those produced by the anionic ROP of cyclotrisiloxanes.

3.3.1.3 Copolymerization

The copolymerization of a functional cyclotrisiloxane with D_3 leads to a copolymer of dimethylsiloxane units and siloxane-containing functional group units which – in similar manner to the copolymer obtained by ROP of cyclosiloxane with mixed units – contains macromolecules of uniform structures with regards to the size, monomer unit composition and sequencing [117]. However, the distribution of units along the chain is different. The more reactive comonomer enters the chain

Table 3.4 Anionic ROP of difunctional cyclotrisiloxanes $R_1R_2SiO(Me_2SiO)_2$.

R_1	R_2	Conditions	Regioselectivity	Reference
Vinyl	Vinyl	$Ph_2Si(OLi)_2$, THF, HMPA, 0 °C	High	[139]
C_6H_5	C_6H_5	Li silanolate, THF K silanolate + 18-C-6, toluene Me_4N^+ silanolate, toluene	Poor	[140]
$OSiMe_3$	$OSiMe_3$	$Ph_2Si(OLi)_2$, THF, HMPA, RT	High	[141]
$(CH_2)_2C_6F_{13}$	$(CH_2)_2C_6F_{13}$	$O(SiMe_2OLi)_2$, THF, RT	High	[142]
H	$OSiMe_2Vinyl$	$Ph_2Si(OLi)_2$, THF, 0 °C	— (+SiH not affected)	[143]
C_6H_5	$C_6H_4CF_3$	$Ph_2Si(OLi)_2$, THF, HMPA, 0 °C	High	[144]
C_6H_5	$C_6H_3(CF_3)_2$	$Ph_2Si(OLi)_2$, THF, HMPA, –20 °C	High	[144]
H	$OSiMe_3$	$Ph_2Si(OLi)_2$, THF, –50 °C	High	[137]

Table 3.5 Anionic ROP of functional cyclotetrasiloxanes.

Monomer	Conditions	Comments	Reference
$(VinylMeSiO)_4$	P_4 - <i>t</i> -Bu superbase, bulk, 80 °C	Random microstructure + cycles	[43]
$(C_6H_5MeSiO)_4$	P_4 - <i>t</i> -Bu superbase, bulk, RT	Very fast propagation	[41]
$(Vinyl)_2SiO(Me_2SiO)_3$	P_4 - <i>t</i> -Bu superbase, bulk, 80 °C	Broad M_w/M_n distribution	[145]
$(C_6H_5)_2SiO(Me_2SiO)_3$	P_4 - <i>t</i> -Bu superbase, THF, 80 °C	Random microstructure + cycles	[146]
$[C_2F_3(CF_2OCFCF_3)_nC(=O)X]MeSiO(Me_2SiO)_3$ where X = O, NH, NMe and $n \sim 3$ or 7	$Bu_4N^+F^-$, THF, heat	Large conversion in polymer	[147]

preferentially, and thus the density of the units from this monomer in the polymer is high at the start of chain formation. The density generally decreases during chain growth as the contribution of the more reactive monomer in the feed decreases, and this leads to a gradient distribution of the functional groups along the copolymer chain. Different systems have been examined under conditions in

Table 3.6 Simultaneous anionic copolymerization of cyclosiloxanes.

M ₁	M ₂	Conditions	Results	Reference
D ₃	VD ₂	<i>n</i> -BuLi, THF, 25 °C	$r_1 = 0.22$; $r_2 = 8.3$	[134]
D ₃	V ₃	<i>n</i> -BuLi, THF, RT	$r_1 = 0.036$; $r_2 = 17.8$	[119]
V ₄	D ₃	Me ₂ SiCH ₂ Li, toluene, DMSO, 22 °C	$r_1 = 0.05$; $r_2 = 8.6$	[148]
V ₄	D ₃	<i>n</i> -BuLi, THF, -40 °C	V ₄ less reactive than D ₃	[149]

Table 3.7 Sequential anionic copolymerization of cyclosiloxanes.

Block A	Block B	Conditions	Reference(s)
PDMS (D ₃)	PVMS (V ₃)	<i>n</i> -BuLi, THF, 22 °C	[150]
PDMS (D ₃)	PVMS (V ₃)	<i>n</i> -BuLi, cyclohexane/THF, RT	[151]
PDMS (D ₃)	PDMS-alt-PVMS (VD ₂)	<i>n</i> -BuLi, THF, 22 °C	[134, 150]
PDMS-alt-PVMS (VD ₂)	PDMS (D ₃)	<i>n</i> -BuLi, THF, 25 °C	[134]
PVMS (V ₄)	PDMS (D ₃)	<i>n</i> -BuLi, THF, [12-C-4], RT	[152]
PDMS (D ₃)	–[MeSi((CH ₂) ₃ Cl)O] _{<i>m</i>} –	BuMe ₂ SiOLi, THF, 25 °C	[123]
PDMS (D ₃)	–[MeSi((CH ₂) ₃ Cl)O(Me ₂ SiO) ₂] _{<i>m</i>} –	BuMe ₂ SiOLi, THF, 25 °C	[123]

which back-biting and chain transfer are negligible; the results obtained are listed in Table 3.6. When the reactivity ratios were determined, the order of reactivity of the monomers was: V₃ > VD₂ > D₃ > V₄.

The sequential copolymerization of cyclosiloxanes is particularly suitable for the synthesis of well-defined diblock and triblock all-siloxane functionalized copolymers. Using a monofunctional initiator leads to diblock copolymers, while triblock copolymers are formed with bifunctional initiators. Some typical examples of AB block copolymers are shown in Table 3.7. It is recommended that the less-reactive monomer be polymerized in the first step, and this is the case of the examples in which D₃ and V₄ are polymerized first. The comonomer should be introduced not later than at 90–95% of conversion of the first monomer, in order to avoid the processes that lead to chain randomization. Those monomers which have func-

tional groups such as vinyl or 3-chloropropyl are more reactive towards the active centers, as compared with D_3 , and therefore the cross-propagation to residual D_3 hardly occurs in the second step of the copolymerization. The same situation occurs in the case of V_4 , which is less reactive than D_3 . However, when VD_2 (which is more reactive than D_3) is polymerized first, the B block of the resultant copolymer is contaminated by VD_2 units [134]. All other AB block copolymers have a high topological purity, a defined size of blocks, and a low polydispersity [117].

AB and ABA block copolymers have been prepared by the sequential addition of hexaphenyltricyclosiloxane and octaphenylcyclotetrasiloxane on a PDMS with one and two lithium silanolate chain-ends, respectively [153–157]. Some redistribution reactions occurred due to the harsh conditions required for the ROP of the perphenyl cyclic monomers. Finally, some multiblock copolymers have been prepared by the anionic equilibrium polymerization of cyclosiloxanes, which leads to a random distribution of different units—that is, diethyl, diphenyl, methylphenyl siloxy units [157], dimethyl, diphenyl siloxy units [158], and dimethyl, methylvinyl-siloxy units [159].

3.3.2

Cationic Polymerization

3.3.2.1 Homopolymerization of Symmetrical Cyclosiloxanes

Few cyclosiloxanes have been polymerized in a cationic manner, although cycles with bulky substituents always lead to polymers where the anionic processes exclusively produce nonreactive (less stranded) cycles by polymer reversion. For example, Furukawa *et al.* failed to prepare fluorinated silicones from tricyclosiloxanes containing ' $C_4F_9(CH_2)_2$ ' moieties, since intensive depolymerization into four-membered cyclics led to a rapid vanishing of the polymer. However, by carrying out a polymerization catalyzed by triflic acid, in bulk and at 50 °C, Furukawa's group generated a polymer with a bimodal distribution, which nevertheless did not undergo reversion even after long reaction times [127]. Another symmetrical tricyclosiloxane bearing a branched perfluorinated group on each silicon atom, namely ' $C_3F_7C(CF_3)_2(CH_2)_2$ ', was also polymerized successfully in bulk, at 100 °C, using triflic acid as a catalyst, and V_2 as the end-blocker, to generate oligomers of about 5000 g mol^{-1} [160]. A particularly bulky monomer, a tetracyclosiloxane obtained from the hydrosilylation of a $[C_{60}]$ fullerene on D_4^H , was polymerized with triflic acid in *o*-dichlorobenzene to generate 65 wt% of a large molar mass polymer ($M_n = 95\,000 \text{ g mol}^{-1}$) [161]. A F_3 monomer was polymerized using the complex catalyst of Jallouli and Saam [79], namely a trimethylsilyltriflate with a *t*-butyl pyridine proton trap. A well-documented study showed that polymer could be obtained in large yield (typically 70%), depending on the *cis-trans* conformation of the monomer, together with a large content of F_6 . The polymerization was proved to be 'living', by virtue of a polymer extension through the addition of a second shot of monomer.

3.3.2.2 Homopolymerization of Asymmetrical Cyclosiloxanes

Both tricyclosiloxanes and tetracyclosiloxanes, where only one Si atom was functionalized by two phenyl groups, were polymerized cationically by the groups of Chojnowski [162, 163] and Weber [44], respectively. The teams each used triflic acid in hexane at 30 °C, and dichloromethane at 25 °C, respectively. For the most strained monomer, microstructure analyses showed that the polymerization proceeded through the silyl triflate moiety, and that the siloxonium ion was only a transient species of the propagation step. In contrast (according to the authors), the polymer derived from the four-membered cyclosiloxane presented a microstructure typical of the chemoselective ring-opening reaction of a siloxonium cation. Similar conclusions were drawn by the same authors for similar tricyclosiloxane [139] and tetracyclosiloxane [145] monomers with two vinyl groups in place of the phenyls, as well as for tricyclosiloxanes bearing perfluorinated phenyl groups [144].

Hexaethylcyclotrisiloxane was polymerized under conventional triflic acid conditions, in the bulk. Vinyl-terminated polydiethylsiloxanes were first generated and fractionated to further prepare and characterize networks of these [164]. A ^{17}O -enriched monomer was likely polymerized at 50 °C, to generate polymers of very high weight-average molar masses (up to $2.5 \times 10^5 \text{ g mol}^{-1}$), the liquid crystal properties of which were characterized using solid-state nuclear magnetic resonance (NMR) spectroscopy [165]. Another singular monomer successfully polymerized by triflic acid is the 1-hydrido-3-vinyl-1,3,5,5,7,7-hexamethyl-cyclotetrasiloxane, which produced polymers of high molar masses without reaction of the vinyl group [132].

3.3.2.3 Copolymerization

Functional PDMS copolymers bearing Si–H moieties inside the polymer backbone were prepared by several teams, with a view to functionalize by hydrosilylation the silicone chains in a second step. The heterogeneous redistribution copolymerization of D_4 and D_4^{H} , using M_2 as a chain-ending agent, produced the expected random copolymers, rather than multiblock ones, even if the polymer/cycle equilibrium was more rapidly established [166]. Redistribution using triflic acid and a methacrylate disiloxane [167] or M_2 [168] also led to low-molar mass polymers ($<10\,000 \text{ g mol}^{-1}$) with 10% to 75% functional groups.

Cazacu *et al.* carried out an heterogeneous copolymerization between D_4 and a diphenyldichlorosilane, in the presence of minute amounts of water necessary to hydrolyze the chlorosilane before the redistribution reaction [169]. An ‘anionite’ (ammonium resin or basic gel) was also introduced into the recipe to capture the HCl released during the reaction. Polymer yields were decreased to 50%, when the content of chlorosilanes was increased to 70%.

3.3.3

Emulsion Polymerization

Functional polysiloxanes were also prepared via anionic polymerization of cycles with three or four $\text{SiO}(\text{CH}_3)\text{R}$ units, where $\text{R} = \text{CH}_2\text{CH}_2\text{CF}_3$ [170], phenyl [171] or vinyl [172]. Similar kinetic features as for the anionic polymerization of D_4 were

found, except for a faster polymerization for the highly strained monomers (sometimes to a point where conversion rose to 100% before falling to the equilibrium state) and a larger final cycle content (but remaining below that observed in bulk). More recently, D_4^H was also polymerized using a cationic process and different surfactant mixtures [173–175]. Here, a good control of the polymerization was achieved using dodecyl benzene sulfonic acid (DBSA) and a nonionic surfactant, although the extensive redistribution of D_4^H into larger cycles was not clearly explained. The best system in terms of rate of conversion and control over the linear chains molecular characteristics was nevertheless achieved by employing fatty phosphonic acids.

The copolymerization of D_4 with methacryloxytrimethoxysilane (MATS) or propylmethacrylate triethoxysilane (PMTS), or with V_4 , was carried out in emulsion with a view to preparing core-shell or composite particles with organic polymers; these are useful in coatings of low water swelling and different smoothness. In one report [176], it was shown that the conversion in monomer while copolymerizing D_4 and V_4 by a cationic process was quite low, because the monomers were ‘creamed’ at the top of the reactor; however, such a drawback was alleviated by using a combination of DBSA and a silicone surfactant [177].

As this subject has not previously been reviewed, the decision was taken to present here the details of different studies on core-shell particles, where PDMS chains are produced by the ROP of cyclosiloxanes (see Table 3.8). Among numerous factors which affect the final particle structure can be included the nature of the seed latex, the sequence of addition (some studies were carried out in batches), the content of the crosslinker, and the ratio between each phase. It can be concluded from these complex studies that, when batch processes proceed with a simultaneous polymerization, it is most likely that homogeneous composite particles will be formed.

Whilst organic polymer seeds are quite readily encapsulated by a PDMS shell (due to surface tension issues), PDMS cores need to be crosslinked and the organic polymer layer made hydrophilic by charged monomers such as (meth)acrylic acid, in order safely to achieve the expected core-shell structure. The grafting of styrene/acrylonitrile (St/AN) onto a poly(butadiene) shell led to a striking change in the structure of the particles, from core-shell to a flocculated, moon-like configuration. One interesting point here concerns the study conducted by Kong and Ruckenstein [99], who rendered the shell of their particles porous by an acid/alkali treatment. Finally, it is worth pointing out a recent study on the generation of multiblock copolymers by the sequenced emulsion polymerization of D_4 and V_4 [172].

3.4 Polycarbosiloxanes

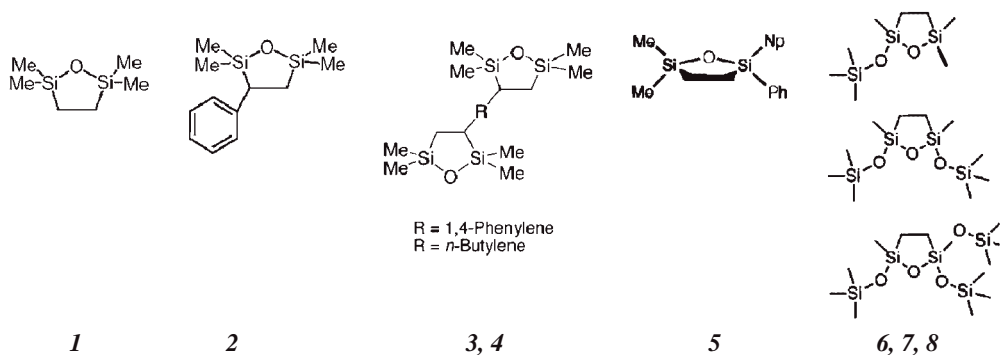
Although silicone polymers show extreme resistance to high temperatures, a low content of a slightly acid or basic impurity may have a dramatic effect on the stability of the chains, which degrade via back-biting reactions. One simple

Table 3.8 Core-shell polymerization with PDMS prepared *in situ*.

Silicone precursor	Organic polymer precursors ^a	Process, conditions	Structure ^b (PDMS cont. wt%)	Reference(s)
D ₄ , PMTS	St, BA	Starved-feed of all monomers SDS + nonionic surfactant, K ₂ S ₂ O ₈ , 80 °C	H (2–10)	[178]
D ₄ , MATS	BA, MAA	Batch or starved-feed of all monomers Surfactant, initiator not specified	H ? (2–15)	[179]
D ₄ , V ₄	BA, MMA, MAA, EGDMA	Batch process DBSA, NH ₄ S ₂ O ₈ , 80 °C	H ? (2–20)	[180]
D ₄ , MATS or V ₄	St	P(S + MATS) seed, D ₄ + crosslinker feed DBSA, γ-irradiation, RT	C _{PS} /S _{PDMS} (30–60)	[177]
D ₄ , MATS, TEOS	BA, MMA, MAA, EGDMA	PA seed, shot or starved-feed additions DBSA, NH ₄ S ₂ O ₈ , 80 °C	C _{PA} /S _{PDMS} (50–90)	[181]
D ₄	BA, MMA, MAA, EGDMA	PA seed, shot additions SDBS + KOH or DBSA, NH ₄ S ₂ O ₈ , 85 °C	C _{PA} /S _{PDMS} (21)	[182]
D ₄ , V ₄	BA, MMA	PDMS seed, post-addition of organic monomers DBSA or nonionic surfactant or silicone surfactant γ-irradiation, RT	H (4–7)	[183]
D ₄ , MeSi(OMe) ₃	St, Bu, AN	PDMS seed, Bu batch polymer, St/AN grafting DBSA, K ₂ S ₂ O ₈ , 70 °C Grafting: SDS, peroxides + reductant, 70 °C	C _{PDMS} /S _{Pbu/AN} M _{PDMS} /S _{Pbu/PS/PAN} (7–38, 50)	[184] [100]
D ₄ , V ₄	St or MMA or GMA (+DVB)	PDMS seed, crosslinking, starved-feed or swelling of monomers NaDBSA + H ₂ SO ₄ , K ₂ S ₂ O ₈ , 80 °C	H(PS/PDMS) SW(PMMA/PDMS) [°] (50)	[185]
D ₄ , V ₄	St or MMA or BMA	PDMS seed, crosslinking or not, shot addition NaDBSA + H ₂ SO ₄ , K ₂ S ₂ O ₈ , 80 °C	C _{PDMSXlinked} /S _{PS} C _{PDMS} / S _{PMMA} or PBMA (50)	[176, 186]
D ₄ , MATS	St, MMA, AA	PDMS seed, starved-feed of monomers DBSA	C _{PDMS} /S _{PS/PMMA/PAA} (10–33)	[99]

a St: styrene, BA: butyl acrylate, MAA: methacrylic acid, MMA: methyl methacrylate, EGDMA: ethylene glycol dimethylacrylate, GMA: glycidyl methacrylate, DVB: divinyl benzene, BMA: butyl methacrylate.

b H: homogeneous composite particles, C: core, S: shell, M: Moon, SW: strawberry.
SDS: sodium dodecylsulfate.



Scheme 3.3

method of preventing this problem is to introduce alkylene groups within the silicone backbone, with the groups spaced at least every four to five D units, and preferentially every two units. The recently acquired results presented here demonstrate the potential to create new generations of chemically-resistant hybrid silicones.

3.4.1

Five-Atom Rings

The most simple cycle is the 2,2,5,5-tetramethyl-1-oxa-2,5-disilacyclopentane (**1** in Scheme 3.3). This and equivalent monomers (structures **2**, **3** and **4** in Scheme 3.3) have been polymerized using different catalytic means. The team of Loy and Rahimian [187, 188] carried out the polymerization of all these monomers using a basic catalyst (i.e. tetrabutylammonium hydroxide; TBAH) and Brønsted acids, namely formic and triflic acids or cationic photoinitiators. Monomer **3**, a solid, was either polymerized in THF or copolymerized with **1**. The polymerization was very fast (<30 min), and resulted in a material that could resist temperatures of up to 500 °C. The authors were confident that these dicyclic monomers, produced via crosslinked materials, would in time replace the conventional sol-gel technique, as the polymerization is straightforward, solvent-free, has less than 5 wt% shrinkage, and generates no porosity in the final material.

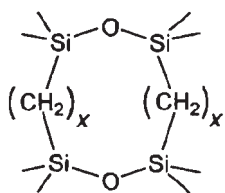
Monomer **1** was also polymerized by a combination of a hydrosilane and a ruthenium catalyst, in solvent and at room temperature, under optimum conditions [189]. Although the molar mass achieved was up to 780 000 g mol⁻¹, the polydispersity was relatively large (up to 3). Acetone, by acting as a chain-terminating agent, allowed these authors not only to characterize their products but also to confirm the transition metal-catalyzed process. Very recently, the IBM polymer group of Hedrick [190] suggested the use of N-heterocyclic carbenes (NHCs) and 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) to polymerize **1** in a controlled fashion, using alcohol or silanol as an initiator. The polymerizations were 'living' and fast, the yields were almost quantitative, and the MMD extremely low (ca. 1.04 under optimized conditions). In particular, TBD prevented the occurrence of redistribution, presumably due to the low pK_b of this molecule.

More complex cyclic carbodisiloxanes were studied by Li and Kawakami [191, 192] and by the group of Weber [193] (see respectively structures **5** and **6**, **7** and **8** in Scheme 3.3). The optically active monomer **5** proceeds to a regioselective polymerization when catalysts such as PhLi, MeONa or *t*BuOK are used, albeit under nonequilibrium conditions: in fact, the redistribution reactions not only decreased the molar mass and yield of the polymer, but also lowered the optical rotation of the polymer due to racemization [191]. A racemic mixture of **5**, when polymerized by PhLi, is stereoselective, while the final polymer is rich in syndiotactic units, which improves its thermostability [192]. Weber polymerized increasingly-substituted siloxydisilacyclopentanes (**6**, **7**, **8**) by using a conventional dilithio diphenyl silanediolate catalyst. Only polymers from **8** produced a stereoregular structure, on the basis of the low molecular weight (5000 versus 50 000 g mol⁻¹ for the two other polymers). The polymer produced also showed a narrow polydispersity, which suggested that the polymerization was ‘living’ or at least off-equilibrium.

3.4.2

Larger Cyclocarbosiloxanes

Two seminal papers [194, 195] described the preparation of tetrasilalkylene cycles, the typical structure of which is shown below. Two techniques were described to prepare these monomers: the first method started from the equivalent dichlorosilane and cyclized the molecule in the presence of a ZnO catalyst; the second method employed the KOH-catalyzed cracking of a polycarbosiloxane polymer of low molar mass, previously prepared by polyhydrosilylation. For large alkylene groups [194], the disilacycle is likely formed, but the ‘double ring’ is crystalline, and so can readily be precipitated and recrystallized.



$$(x = 1, 6, 8, 10, 14)$$

All of these cycles were polymerized using a cationic polymerization process, with triflic acid or ion-exchange cationic resins. The smallest ring ($x = 1$) gave a polymer of about 50 000 g mol⁻¹ with a low MMD (typically 1.4–1.8).¹⁾ Larger cycles

1) The 1,1,3,3,5,5,7,7-octamethyl-2,6-dioxo-1,3,5,7-tetrasilacyclooctane ($x = 1$) was also polymerized in miniemulsion, using DBSA as a catalyst, to reach polymers of about 70 000 g mol⁻¹ and equivalent MMD after 2 days of polymerization at 50 °C [Ganachaud, F. and Interrante, L.V. (2002), unpublished results].

could achieve polymers of M_n up to $130\,000\text{ g mol}^{-1}$, which was several-fold larger than those obtained for the equivalent disilacycle, and with wide polydispersity (>2). The glass transition temperature (T_g) was increased by increasing the size of the alkylene spacer, from -106°C for $x = 1$ to -70°C for $x = 12$; melting points around 0°C were apparent for $x > 6$. Recently, it has been shown that, under an inert atmosphere, poly(dimethylsilylenemethylene-co-dimethylsiloxane) is more resistant at high temperature than PDMS, due to limited reversion reactions, and that a char of 17% was still available at 1000°C ; in contrast, when under air the degradation started at a lower temperature [195].

3.5

Summary and Prospects

In this chapter we have attempted to describe the wide diversity of studies devoted to the ROP of cyclosiloxanes, despite the ‘old age’ of the process and its recognized longstanding efficiency. The major challenge remains the control of polymerization for the cheapest cyclosiloxane, namely D_4 , under not too-restrictive reaction conditions and with a quantitative polymer yield. Yet, the results of recent studies conducted with superbases and heterocyclic carbenes suggest that the quest towards this ‘Holy Grail’ continues.

Besides its academic purpose—namely, to provide a better understanding of the mechanisms of polymerization—the use of partially substituted cycles represents an excellent opportunity to control both the microstructure and the (large) molar mass of polymers; such control is especially beneficial in the case of monomers with large substituents that are minimally polymerized with an anionic catalyst but significantly with cationic catalysts.

Today, although polymerization mechanisms in emulsion processes are well understood, an even deeper understanding of the physico-chemical concepts of these systems might allow one to avoid the pre-emulsification steps which are invariably required. Alternatively, it might be possible to derive conditions to work off-equilibrium; such a feature has been observed when polymerizing F_3 [170], and may in time become routine for other tricyclosiloxanes.

Another, as yet minimally investigated, topic is that of alternated silicon-based copolymer production, using dimethylsiloxo and silazane [196] or silane [197] units, where future interest will surely lie in ceramics or optical activity, respectively.

Finally, certain exotic cycles which, at present, remain resistant to ROP include the tri- or tetra-cyclosilicates (as prepared by Weber and colleagues [198]), and the octaethyl-2,6-dioxo-1,3,5,7-tetrasilacyclo-octane (as developed by Interrante and coworkers [195]). The task here will be to identify those highly active catalysts which, apart from opening such cycles, can be used to optimize conditions for the nonequilibrating polymerization of D_4 ; if this becomes feasible, it should indeed be possible to ‘loop the loop’!

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4

Sulfur–Nitrogen–Phosphorus-Containing Polymers*Frederick F. Stewart and Eric S. Peterson*

4.1

Introduction

The synthesis and study of heterocycles containing main-group elements has played a pivotal role in the development of inorganic chemistry. Well-known classes of inorganic rings include the cyclic phosphazene (Figure 4.1), which was first prepared by Liebig and Rose [1, 2] in 1834, and borazines, the initial example of which was first synthesized by Stock and Pohland [3] in 1926. A further inorganic ring example is provided by sulfanuric chloride [4], which has been known since the 1950s. It is noteworthy that the ring skeletons in phosphazenes and borazines have been shown to be very robust and to permit facile halogen atom replacement reactions [5]. This chemistry has been well studied and has provided much useful information on nucleophilic substitution reactions in inorganic chemistry.

The bonding used to describe these structures such as those found in Figure 4.1, and the possible application of the label ‘inorganic benzene’, has been the subject of much debate. Current research continues to uncover fascinating new ring systems that pose intriguing questions with respect to their bonding, or that exhibit unexpected reactivity. Some noteworthy examples include 6p-electron gallium-based systems and pseudo-aromatic cyclic silylenes [6, 7], novel cyclic tellurium imides [8], and interesting aluminum–pnicogen heterocycles [9], among others [10]. One of the primary reasons for studying inorganic rings is their well known use as precursors for polymers and solid-state materials. The synthesis of long chains of atoms of inorganic elements—inorganic polymers—provides a substantial synthetic challenge, but is motivated by the possibility of accessing new materials with interesting and useful properties [11]. The most well-known and widely used current routes to high-molecular-weight polysiloxanes [12], polyphosphazenes [13–15] and poly(carbosilanes) [16, 17], involve a ring-opening polymerization (ROP) reaction. With this in mind, interest in the polymerization behavior of other inorganic rings has recently gathered momentum. Polysilanes [18], poly(carbophosphazenes) [19] and poly(thiophosphazenes) [20] represent examples

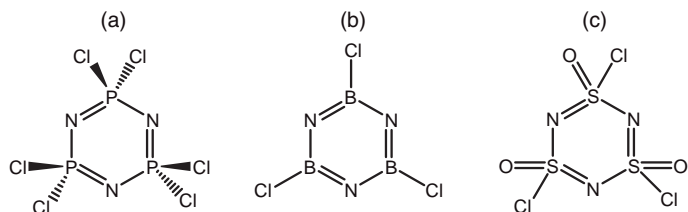


Figure 4.1 Cyclotriphosphazene (a), borazine (b) and sulfanuric chloride (c).

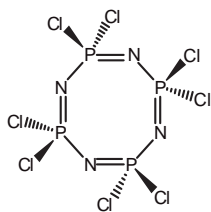


Figure 4.2 Octachlorocyclotetraphosphazene.

of well-characterized polymers, which have been successfully prepared by ROP during the past two decades. The use of inorganic rings to construct solid-state materials with novel properties has also been successfully developed. For example, materials with interesting electronic, magnetic and conductive properties have been prepared from sulfur–nitrogen or selenium–nitrogen heterocycles [21, 22]. In addition, inorganic rings have attracted considerable attention as precursors to ceramics via thermolysis: examples include the use of aluminum–nitrogen or gallium–arsenic heterocycles to prepare AlN and GaAs, respectively [23, 24]. This chapter focuses upon three broad topical areas that include the ring-opening polymerization chemistry of: (i) halogenated cyclotriphosphazenes; (ii) nonhalogenated phosphorus–nitrogen rings; and (iii) the incorporation of sulfur into the phosphorus–nitrogen rings and their polymerization chemistries.

4.2

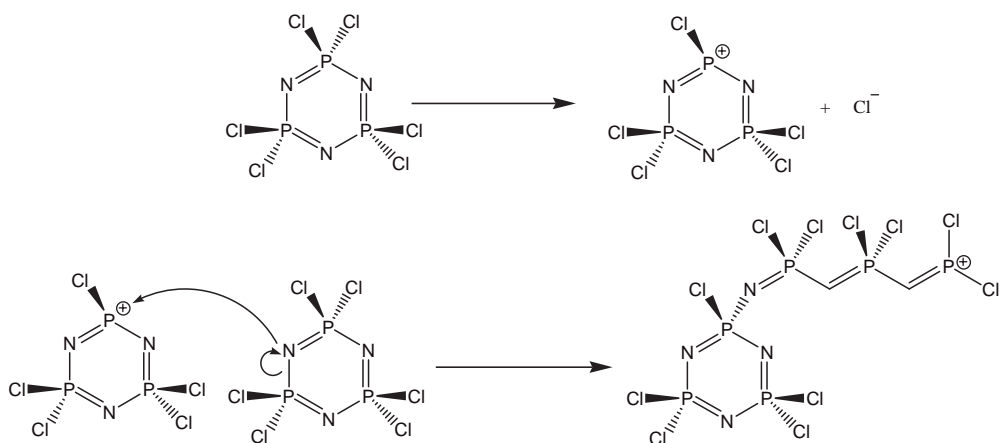
Mechanism and Methods in Ring-Opening Polymerization (ROP) of Halogenated Cyclotriphosphazenes

An effective summary of the early state of phosphazene chemistry, and in particular, the ROP of hexachlorocyclotriphosphazene and octachlorocyclotetraphosphazene (Figure 4.2) was published in 1962 [25]. These studies were dominated by the substitution chemistry of these small rings; however a section was dedicated to a summary of the available knowledge in polymerization chemistry in these systems. To this point, the chemistry of these systems is dominated by studies into polymerized intractable ‘inorganic rubber’, obtained from the uncontrolled ROP of phosphazene rings.

Contemporary to this review were studies examining the mechanism of the polymerization performed both, with and without, added catalysts. The reaction

rates and kinetics studies of hexachlorocyclotriphosphazene polymerization in both solution (in CCl_4) and in bulk (solvent-less) have yielded second-order kinetics and an activation energy of 42 kcal mol^{-1} for the uncatalyzed bulk polymerization [26, 27]. Further, there appeared to be no clear difference kinetically between the trimer and the tetramer. Konecny studied the catalyzed bulk reaction at 211°C using a variety of organic additives including benzoic acid, ethanol, diethyl ether, diethylamine, di-*tert*-butyl peroxide and acetone [28]. Inorganics added to this study were tin, water and ammonia. All of the organics were found to catalyze the reaction and to exhibit higher reaction rates, except for the peroxide, which was found to be catalytically inactive; this suggested that the polymerization did not proceed through a free-radical mechanism. Tin was also found to be inactive; however water and ammonia, with their ability to react directly with the phosphazenes to form adducts, also were inactive and led to unwanted side products. The behaviors of these potential catalysts led the authors to suggest that only those species that can interact or otherwise facilitate chloride removal from the trimers were effective candidates for catalysis. Alcohols, ethers and organic acids would facilitate ring opening, whereas saturated hydrocarbons and alkyl halides would be catalytically inert.

The solution polymerization of trimer in benzene was used to further delineate the catalytic role of small oxygen-containing organic species [29] such as benzoic acid, diethyl ether, methanol and acetone. Catalysis with benzoic acid was found to follow first-order kinetics with respect to trimer, and demonstrated a positive rate enhancement with increasing loadings of catalyst. Diethyl ether, while also exhibiting first-order kinetics, differed strongly from benzoic acid in that a long induction time was observed before polymerization occurred; in addition, the rate of reaction was observed to be independent of the catalyst concentration. Methanol, on the other hand, exhibited behavior similar to that of benzoic acid in showing first-order kinetics, however the catalyst effect was proportional to the amount of added catalyst. Acetone exhibited a limited catalytic activity and provided a basis for an estimation of the initial rate, which was clearly similar with all organics that gave a catalytic effect. To the authors, this suggested that the mechanism of the reaction was essentially the same, regardless of the catalyst employed. Thus, an evaluation of the catalysts showed that the more effective catalysts had active groups such as alcohols and acids that would react readily with trimer at room temperature. The data suggest that polymerization proceeds through an initial reaction of the organic with the trimer to yield a catalytically active species, followed by a slow polymerization in which the active species reacts with and opens other trimer rings to yield a linear polyphosphazene structure. Given the fact that HCl is evolved during the polymerization, species with donor protons such as benzoic acid and methanol would be expected to facilitate the loss of chloride, yielding an active cationic species (Scheme 4.1). A subsequent attack by nitrogen lone-pair electrons on the phosphorus cation yields a new P-N bond with concurrent cleavage of an existing P-N bond, leading to ring opening to obtain a linear phosphazene. The lower catalytic activity of aprotic organics such as acetone and diethyl ether provides additional support for a cationic polymerization mechanism.



Scheme 4.1 Proposed cationic mechanism for the polymerization of hexachlorocyclotriphosphazene.

An additional interesting observation was the observed fivefold increase in reaction rate observed in bulk polymerizations, as opposed to solution. Taking into consideration the densities of the respective systems, and considering the catalyst loading on a volumetric basis instead of a weight basis, gives an only two- to threefold increase in the rate of the bulk system. From this, the authors proposed that an aprotic benzene solvent played no significant role in the polymerization mechanism.

A further exploration of the benzoic acid-catalyzed bulk polymerization was presented by Gimblett [30]. As an extension of the studies conducted by Konecny, the polymerization of trimer catalyzed by benzoic acid was performed at temperatures ranging from 200 to 220 °C. With increasing temperature, the rate of polymerization was also observed to increase, and an Arrhenius treatment of the data yielded an activation energy of 24.3 kcal mol⁻¹. The induction time mentioned by Konecny for diethyl ether catalysis was also observed in these experiments, decreasing in duration with increasing temperature. The first-order dependence was found to be valid only between 0 and 60% conversion; at degrees of polymerization greater than 60% the rate was found to fall below that of first order, which the author ascribed to an increasing viscosity and the onset of gelation.

Patat claimed, in an early study, that oxygen plays a role in the mechanism of trimer polymerization, although the role was not clearly defined [26]. Later investigations performed *in vacuo* suggested that oxygen does not necessarily play an important part in the polymerization reaction [30]. Parallel experiments performed at 210 °C, both in the presence of oxygen (400 mmHg) and evacuated (10⁻⁴ mmHg), resulted in near-identical polymerization in terms of overall polymerized yield and gel formation. Gel formation is seen primarily at conversions in excess of 70%.

Gimblett also paid some attention to the morphology of the resulting polymer materials [30]. It was assumed that gelation necessitated branching, and that

catalysts which are active in facilitating the removal of chlorine could also pull multiple chlorines from a single ring; this would result in numerous new P–N bonds and a branched polyfunctional structure. However, the supposition of branching being induced by catalyst loading was not supported by the data obtained.

MacCallum argued for a cationic polymerization mechanism through studies of bulk polymerization, both with and without benzoic acid catalysis, at temperatures ranging from 240 °C to 255 °C [31]. Consistent with the Gimblett report, an increasing temperature increased the rate of polymerization; however, it was asserted that a second-order fit of the kinetic data was a better treatment, consistent with the earlier report by Patat. One significant difference from Patat, however, was the activation energy, which was calculated to be significantly larger at 57.1 kcal mol⁻¹. It should be noted that this study concentrated on the polymerization of trimer to polymer at a limit of 30% conversion, presumably to avoid gelation issues associated with higher conversions.

In order to probe the intriguing catalytic behavior of benzoic acid, studies were conducted with the acid and the sodium salt, sodium benzoate, to determine the whether the protic nature of the catalyst was significant [31]. Complete dissociation of the acid in the molten trimer under reaction conditions was viewed as a matter of speculation, and the presence of protons did not provide any clear insight into the role of the benzoate ion. Sodium benzoate was safely assumed to be dissociated. The data recorded for both catalysts suggested similar kinetic behavior, which in turn implied that the potential degree of ionization of the catalyst does not play a role in the catalysis.

In these studies, the analysis of off-gas products was also found to provide insight into the chemistry of this ROP process. The breakdown products of benzoic acid found in the off-gas included benzoyl chloride and benzonitrile. At low polymer yields, the only additional species found was HCl, formed from the acidic proton and chlorine liberated from the trimer. In this study, the relative amounts of each constituent were not obtained due to low concentrations; however, the authors observed that the benzoic acid was consumed relatively early in the polymerization. The small difference in the rates of catalysis for both the acid and the sodium salt also supported a quick reaction to some derivative compound; however, no structure was proposed for this compound.

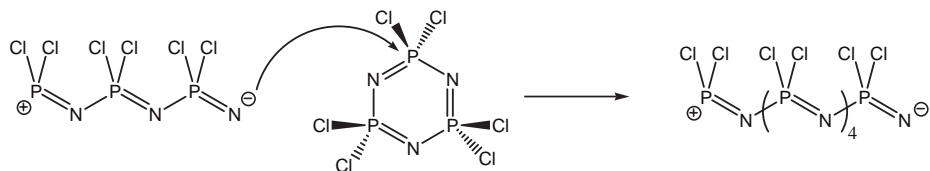
Finally, the effect of water on polymerization was studied. The introduction of increasing amounts of water into the polymerization tubes resulted in higher degrees of polymerization, although the polymer—which normally is a white solid—turned first brown and then black. Furthermore, the solids became increasingly insoluble as a function of water content.

From these data, MacCallum proposed an equilibrium between the closed trimer and the ring-opened oligomers (Scheme 4.2). Polymerization would then occur through a nucleophilic attack from the nitrogen anion onto a phosphorus from an adjacent ring, which then regenerates the anion and doubles the chain length (Scheme 4.3).

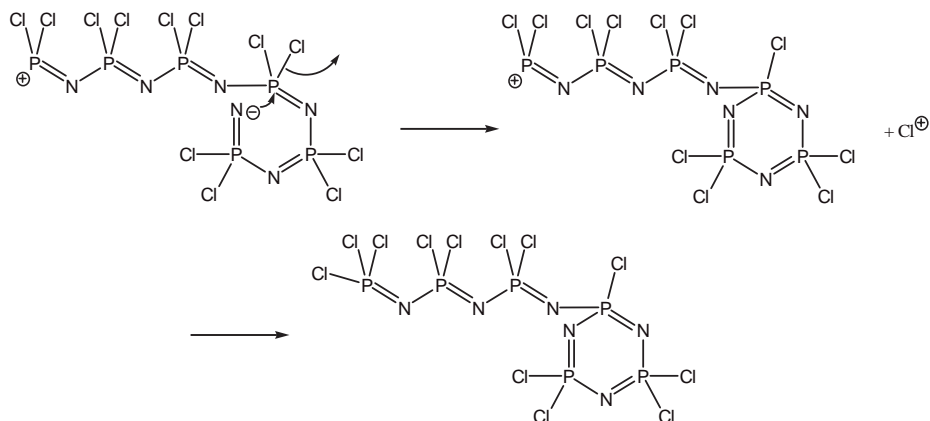
Under this scenario, polymerization does not yield a loss of chlorine. Hence, MacCallum proposed that intramolecular ring closing would yield both



Scheme 4.2 The initiation of trimer polymerization.



Scheme 4.3 The propagation step.

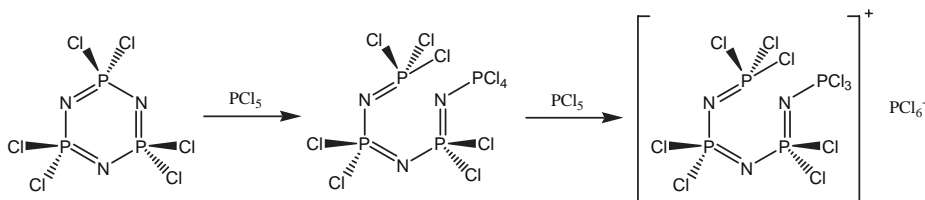


Scheme 4.4 The termination steps.

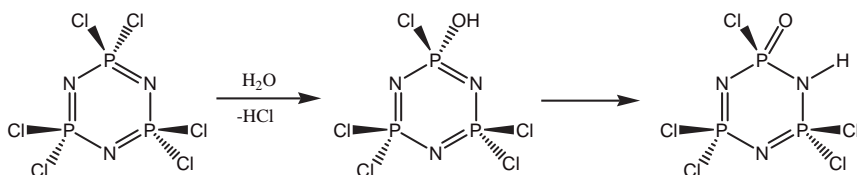
termination of the polymerization and liberate chloride, which could also participate in the termination (Scheme 4.4).

Further studies on identifying the role of other potential contaminants, such as PCl_5 , water and HCl , on ROP were reported by Allcock in 1975 [32]. These investigations were driven by the observation that the polymerization does not appear to proceed below 230°C and that, above this temperature, the visual polymerization rate can be erratic. In this report, a significant observation was made concerning an uncatalyzed reaction in which molecular weight determinations of unsubstituted products were performed. No low- (oligomeric) or medium- (<3000mers) molecular weight fractions were observed, which suggested that, once an initiation event occurs, polymerization to a high-molecular-weight material (3000–30 000mers) proceeds rapidly.

The effect of the presence of PCl_5 was studied as this might be carried over from the trimer synthesis chemistry. PCl_5 was found to inhibit the polymerization, and



Scheme 4.5 Reaction of hexachlorocyclotriphosphazene with PCl_5 .



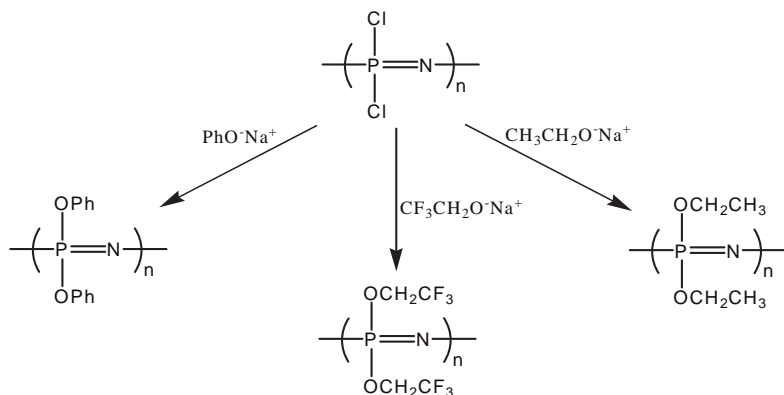
Scheme 4.6 Reaction of hexachlorocyclotriphosphazene with water.

at lower PCl_5 concentrations no polymerized products were observed. However, at higher concentrations it was suggested that the PCl_5 could react with the trimer, resulting in a nonpolymerizable species (Scheme 4.5).

Like PCl_5 , HCl was found to reduce the rate of polymerization with increasing concentrations. HCl is always present in the polymerization process unless water is scrupulously excluded. Thus, the role of water also was studied. It is known that hexachlorocyclotriphosphazene undergoes hydrolysis in the presence of significant amounts of water to yield oxo-phosphazenes, which facilitates ring cleavage through additional hydrolysis (Scheme 4.6). Once the ring structure is disrupted, the hydrolysis process continues, ultimately yielding ammonia, phosphoric acid and HCl . Traces of water, on the other hand, were found to be catalytic in that rate enhancements were observed, consistent with the MacCallum study. Amounts considered as traces were 0.02 to ~0.1 mol% water.

Perhaps the most significant breakthrough in practical phosphazene chemistry was the ability to polymerize hexachlorocyclotriphosphazene to obtain *soluble* linear poly(dichlorophosphazene) in a somewhat reproducible manner; moreover, the polymer could be stabilized by immediate reaction with organic nucleophiles. H. Allcock first reported on the subject of the ROP of hexachlorocyclotriphosphazene and octachlorocyclotetraphosphazene in 1964 [33], when he and Best described the synthesis and studied the mechanism using electrochemical methods and electron spin resonance (ESR).

Prior to the report made by Allcock and Kugel in 1965 [34], numerous attempts at generating hydrolytically stable, completely substituted and soluble materials had failed [35–38]. However, in this latest report the first polymerization of soluble poly(dichlorophosphazene) and a strategy for substitution forming poly(organophosphazenes) was described. The method entailed formation of the linear soluble poly(dichlorophosphazene) by heating at 250°C under vacuum. The amount of time required for polymerization was found to vary up to 48 h, as the reaction was extremely sensitive to trace impurities. Polymerizations are typically



Scheme 4.7 Examples of substitution of poly(dichlorophosphazene).

performed in thick-walled glass polymerization tubes, with the extent of reaction being monitored by observing the melt viscosity. Initially, hexachlorocyclotriphosphazene melts at approximately 113 °C and has a low viscosity, similar to that of water as observed in the polymerization tube at 250 °C. As the polymerization progresses, the viscosity is observed to increase significantly and, if not monitored, the melt will completely stop flowing—at which time it is more likely to yield crosslinked, intractable polymer. The removal of heating at the point at when the viscosity is high and the flow of molten material is slow as the tube is inverted, results in the production of a mixture of poly(dichlorophosphazene) of various molecular weights and unreacted hexachlorocyclotriphosphazene. The separation of these components can be accomplished by removal of the material from the cooled tube, dissolution in anhydrous toluene, followed by precipitation into hexane. In this process, the polymerized phosphazene is physically collected as a swollen gum, while the unreacted hexachlorocyclotriphosphazene and lower-molecular-weight oligomers and polymers remain dissolved in the solvent. Repetition of this procedure at least once is required for complete removal of the trimer/oligomers from the high-molecular-weight rubber.

Once purified, the poly(dichlorophosphazene) must be immediately dissolved in an anhydrous solvent (preferably toluene) in order to be kept stable, and should be used within two to three days. Key to maintaining the polymer as a soluble rubber is preventing its exposure to moisture. This was recognized by Allcock in 1965 [34], when the lability of the phosphorus–chlorine bond was exploited to obtain hydrolytically stable polymers (Scheme 4.7). Exposure of the soluble polymer to sodium trifluoroethoxide, sodium phenoxide and sodium ethoxide yielded the expected polymers, all of which were found to have their chlorines displaced.

Other methods of polymerization have met with mixed results, but are worthy of mention at this point. Studies of the photochemical initiation of hexachlorocyclotriphosphazene polymerization were conducted by Dishon and Hirshberg [39]. The exposure of hexachlorocyclotriphosphazene in solvent to ultraviolet irradiation was found to yield both soluble and insoluble products. Although the solutions

were initially clear, on prolonged exposure they turned brown and formed gelatinous precipitates that were found to be completely insoluble in typical organic solvents. The precipitates were also found to be insoluble in acids, but were consumed in hot nitric acid. Among the soluble components, no increase in solution viscosity was observed, arguing against a clean, high-yielding polymerization.

The plasma polymerization of phosphazene monomers was the subject of a 1982 U.S. Patent [40], wherein the phosphazene monomers studied were trimers and tetramers substituted with halides or organic nucleophiles. Experiments were conducted by direct exposure of crystalline trimer to the plasma, followed by extraction of the residues into warm tetrachloroethane. It was concluded that the resultant polymers were crosslinked and formed in low yield (~10%). Another experiment used an initial plasma polymerization followed by post-plasma treatment at 210°C. On comparison with a control sample which was subjected only to the post-plasma treatment, some polymerization was observed, although the only residues formed were insoluble in toluene.

Catalysis of the polymerization of trimers with Lewis acids such as BCl_3 has been extensively studied in an attempt to obtain reproducible polymerizations at temperatures as low as 150°C [41, 42]. In these studies, which featured the thermal polymerization of hexachlorocyclotriphosphazene in 1,2,4-trichlorobenzene solution, the observed initial rate, degree of polymerization and the molecular weight of the product were each found to depend on the concentration not only of BCl_3 but also of the trimer in solution as well. Although the addition of small amounts of water to the BCl_3 catalyst had no effect on the apparent reaction rate, increasing amounts of water actually inhibited the polymerization. Such inhibition was attributed by the authors to a reaction of the BCl_3 with water to yield a noncatalytic boric acid.

Another BCl_3 -containing catalyst that was found to successfully catalyze the polymerization was the organophosphorus adduct $(\text{RO})_3\text{POBCl}_3$ [43]. In order to determine whether the phosphorus plays a role in the catalysis, $(\text{C}_6\text{H}_5\text{O})_3\text{PO}$ was studied without any apparent catalysis [42]. In fact, $(\text{C}_6\text{H}_5\text{O})_3\text{PO}$ showed an opposite effect in that, at 42 mol%, no polymerization was observed after 300 h at 225°C. But, under these same conditions without the phosphate, a conversion of 40% was observed after 100 h. Phosphates, in this application, can be thought of as Lewis bases. Other Lewis bases, such as DABCO (1,4-diazabicyclo[2.2.2]octane), urea and triphenylphosphine, also completely inhibited the polymerization. From these data it can be concluded that Lewis acids promote catalysis by chlorine abstraction to initiate ring-opening, thus suggesting a cationic mechanism.

Other initiators that have the potential to assist in the extraction of chlorine from the trimer ring, leading to useful polymerizations, have also been examined [44], including triphenylphosphine (PPh_3) and partially substituted trimers (Figure 4.3). Benzoic acid was also revisited in addition to hydrated metal salts that were used to tightly control the water content. From these data, the phosphazene rings appeared to provide the greatest amount of soluble high polymer, although higher loadings of benzoic acid also provided greater conversions. However, these experiments tended to produce polymers with low molecular weights, which may account

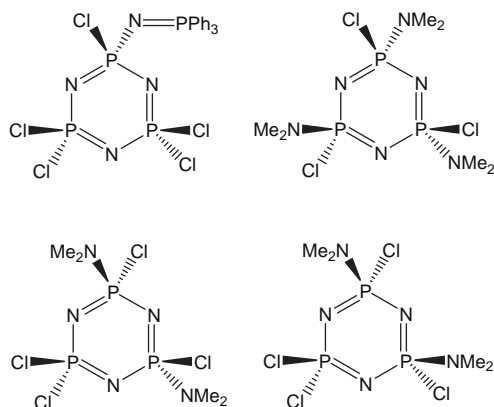
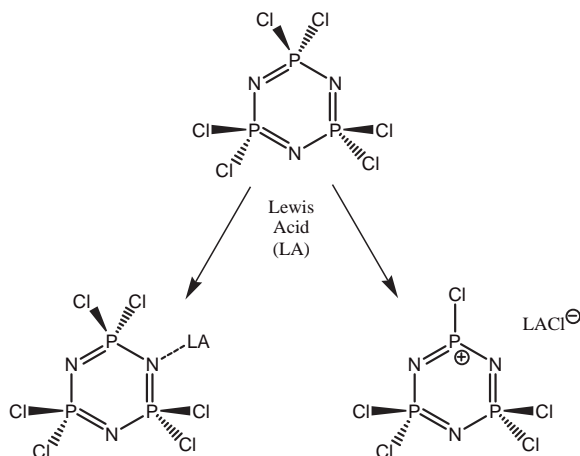


Figure 4.3 Trimer catalysts.



Scheme 4.8 Potential chemistries between a Lewis acid and hexachlorocyclotriphosphazene.

for the higher percentages of soluble materials. With PPh_3 as an initiator, low conversions to polymerized material with low molecular weights were obtained. Thus, the nature of the catalyst appears not to affect the fundamental chemistry and the nature of the resulting products.

In the polymerization reaction, the removal of chloride is a necessity for the cationic mechanism to operate. A variety of attempts have been made to characterize reaction products between a Lewis acid and hexachlorocyclotriphosphazene, using approximately stoichiometric amounts of catalyst. Lewis acids, such as VOCl_3 and AlBr_3 were found to form stable adducts to hexachloro- and hexabromocyclotriphosphazene, rather than the desired charge-separated cationic structures (Scheme 4.8) [45, 46].

Further studies have yielded crystallographic and nuclear magnetic resonance (NMR) evidence favoring addition, as opposed to chlorine abstraction [47]. In these studies, AlCl_3 and GaCl_3 were used as the added species and, in all cases, the

authors reported addition of the Lewis acid at the ring nitrogen atoms. To aid in the characterization, cyclotriphosphazenes were synthesized with ^{15}N labeling, which made the atom's spin—when coupled to other nearby spin $1/2$ nuclei—directly observable by using NMR spectroscopy. The GaCl_3 adduct was found to have a broad ^{31}P resonance at 23.4 ppm with a shoulder at 23.3 ppm, suggesting a fluxional solution state structure. The AlCl_3 resonance was slightly more upfield at 24.6 ppm and even more broad than the GaCl_3 analogue, which suggested that fluxionality was more significant for the AlCl_3 example. ^{15}N NMR revealed upfield shifts for both adducts with respect to hexachlorocyclotriphosphazene, indicating complex formation. Aluminum also is observable with NMR spectroscopy; for the AlCl_3 adduct, a broad signal at 107.1 ppm was observed, which was consistent with a four-coordinate aluminum center. A significant aspect of these adducts is that they were only stable in solution at -60°C , as higher temperatures lead to their degradation.

Key to the characterization of these species was the crystallographic data, especially the Al (and Ga)–N bond length measurements which, by comparison with reported values, indicated direct coordination. It was also apparent that, upon addition of the Lewis acid, the ring distorted somewhat from a planar to a chair-like structure. The structure of these complexes could be best described as fluxional dative bonding with no removal of chlorine. In a similar study, the chemistry of electrophilic carborane reagents in contact with hexachlorocyclotriphosphazene was studied [48]. These reagents, $\text{CHB}_{10}\text{R}_5\text{X}_6^-$, where $\text{R} = \text{H}$ or Me and $\text{X} = \text{Cl}$ or Br , were chosen because they are more potent reagents than those based on other noncoordinating anions (e.g. triflate), and the large nature of the anions encourages crystallization. Cations associated with the carboranes included methyl cations, protons and silylium species (Me_4Si and Et_4Si), all of which are known to be potent dehalogenation agents. However, in all cases the desired phosphazene cations were not obtained. NMR spectroscopy results suggested—consistent with earlier reports—the formation of adducts at nitrogen, and this was later supported by X-ray crystallographic studies. Furthermore, NMR data indicated that the protonated adduct showed significant fluxionality and that protons could ‘hop’ between protonated and nonprotonated rings. Once again, attempts to isolate the active cationic species that has been proposed as being responsible for ROP were unsuccessful.

4.3

Ring-Opening Polymerization and Chemistry of Nonhalogenated Phosphazene Rings

So far, discussions of the ROP of cyclic phosphazenes have been limited to halogenated rings. Yet, there was a desire to develop a simplified route to poly(organophosphazenes) by performing nucleophilic substitution chemistry on the more labile trimer followed by polymerization; this had the advantage that, in general, the substitution chemistry would be quicker and easier when performed

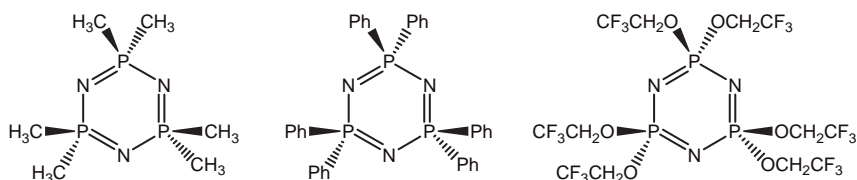


Figure 4.4 Structures (let to right) for hexamethylcyclotriphosphazene, hexaphenylcyclotriphosphazene, and hexa(2,2,2-trifluoroethoxy)cyclotriphosphazene.

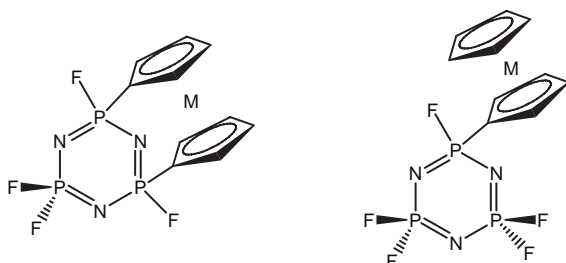


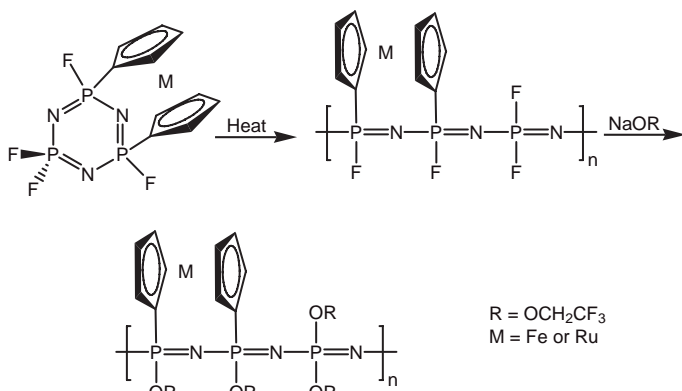
Figure 4.5 Structures for mono- and bidentate attachment of metalocenyl pendant groups on to a fluorinated cyclotriphosphazene ($M = \text{Fe}$ or Ru).

on trimer rings, as opposed to linear phosphazene polymers. Trimer rings bearing organic pendant groups such as methyl, phenyl and 2,2,2-trifluoroethoxy (see Figure 4.4) do not readily polymerize under thermal conditions [49–51].

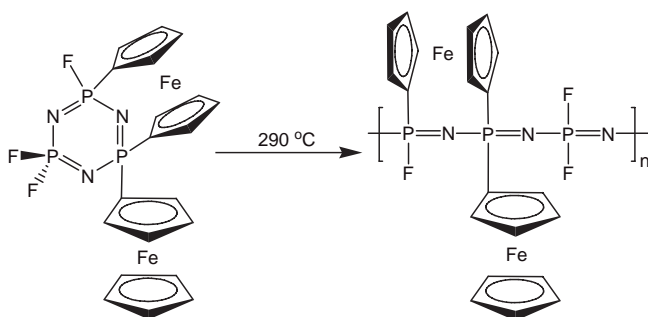
In their investigation of trimer rings with organometallic substituents, Allcock and coworkers found that certain trimers with either metalocenyl substituents (Figure 4.5) could polymerize under thermal conditions [52]. The polymerization of hexafluorocyclotriphosphazene required heating to 350 °C, whereas bidentate metalocenyl trimers were found to polymerize 100 °C lower (at 250 °C), suggesting an activation of the trimer ring to the polymerization process.

The monodentate examples were seen to differ in terms of their polymerization behavior from the bidentate species. Although the monodentate ruthenocenyl derivative was found to polymerize, albeit at a higher temperature (300 °C) than the bidentate derivative, changing the metal to iron caused no polymerization to be evident and the trimer decomposed at 300 °C. Lowering the temperature to 250 °C failed to produce any polymerized products, even after a 17-day reaction time. However, polymerization at 250 °C was accomplished by the addition of 0.1 mol% hexachlorocyclotriphosphazene as catalyst. All linear polymers were treated with 2,2,2-trifluoroethoxide (as the sodium salt) to remove labile fluorines and create stable materials for analysis (see Scheme 4.9).

As a study of the inhibition effect of the monodentate ferrocenyl linkage, a trimer was prepared containing both the polymerizable bidentate and monodentate pendant groups [53]. This mixed trimer was polymerized readily at 290 °C



Scheme 4.9 Polymerization scheme for bidentate metallocenyl trimer derivatives.

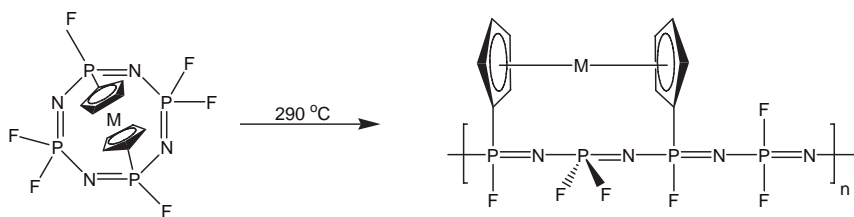


Scheme 4.10 Polymerization of a bis-ferrocenyl phosphazene trimer.

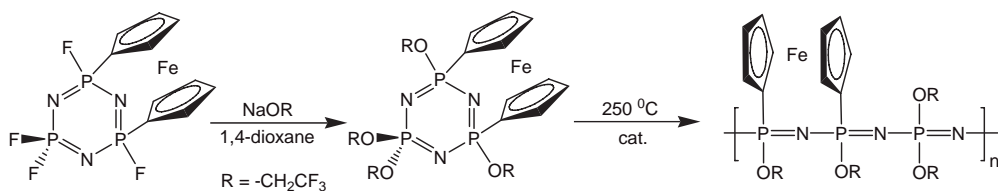
(Scheme 4.10), and subsequent reaction with sodium 2,2,2-trifluoroethoxide yielded a hydrolytically stable polymer suitable for characterization. Thus, while the monodentate ferrocenyl pendant group does not prevent polymerization, the bidentate group may encourage it.

Intriguing structures also were devised using tetrameric phosphazenes in which ferrocenyl linkages were established across two mers (Scheme 4.11). It is significant to note that this chemistry was possible for both metals, and that it is reasonable that the 1,3-substituted metallocenyl functionality has a significant effect on the conformation of the phosphazene tetramer. In fact, it was proposed that conformational ring strain may play a role in the ability to achieve polymerization at the temperature at which it occurs [53].

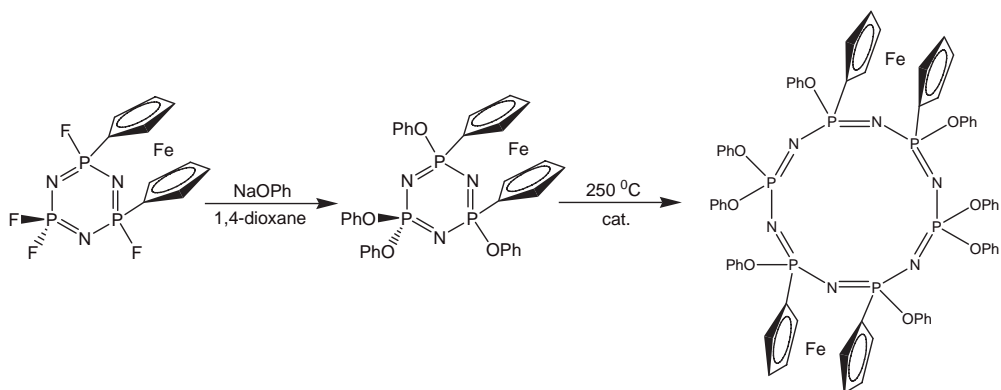
In recognizing the role of ring strain, Allcock and colleagues were able to exploit metallocenyl-substituted phosphazene trimers to achieve the polymerization of rings that contained no halogens [54]. This was significant because, before this report, nobody working in this field had discussed the successful polymerization of a nonhalogenated phosphazene trimer/tetramer. Yet, if it were possible to polymerize organocyclotriphosphazenes, this would greatly simplify the polymerization process by providing a stable precursor.



Scheme 4.11 Synthesis of 1,3-substituted metallocenyl polyphosphazenes.



Scheme 4.12 ROP of a nonhalogenated ferrocenyl trimer.



Scheme 4.13 Ring expansion of tetraphenoxy ferrocenyl phosphazene trimer.

Substitution of the bidentate ferrocenyl fluorinated trimer with sodium 2,2,2-trifluoroethoxide yielded the expected trimer with the fluorines completely displaced (Scheme 4.12). Subsequent direct polymerization of this trimer at 250 °C for 14 days failed to yield any polymer, although higher oligomeric cyclic compounds were detected. However, the addition of 1 mol% hexachlorocyclotriphosphazene as a catalyst resulted in polymerization of the trimer.

Similar reaction chemistry was attempted with the phenoxide-substituted analogue, but no polymerization was observed, even with addition of a catalytic amount of hexachlorocyclotriphosphazene (Scheme 4.13). The major product isolated under catalytic conditions was the ring-expanded cyclohexaphosphazene, with small amounts of cyclononaphosphazene and cyclododecaphosphazene. The difference in chemistries between $-\text{CH}_2\text{CF}_3$ and $-\text{OPh}$ suggests that the steric demands of the pendant groups play a role in the ability to form macromolecular

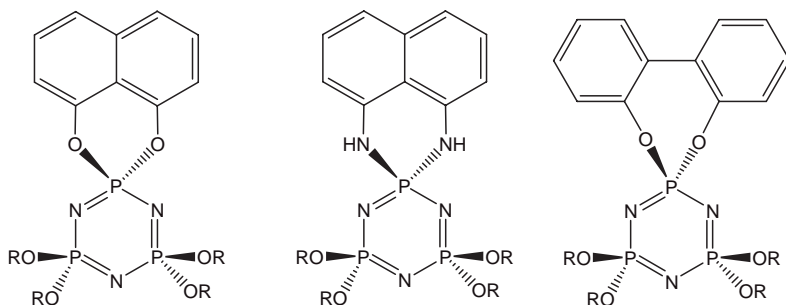


Figure 4.6 Various spirocyclic (1,1-disubstituted) phosphazene trimers ($R = -CH_2CF_3$).

structures. In oligomeric systems—where these steric demands are greater—intramolecular crowding can actually impede the formation of linear polymer. Whilst it is possible that this chemistry might be providing a glimpse into the complex chemistries that occur during polymerization, these study results clearly support the proposition that trimer/tetramer ring strain can encourage ROP.

A further exploration of this chemistry was performed to probe the relationship between the organic ring substituents and their resulting polymerization behavior [55]. Both, methyl and phenyl groups were added as substituents and the polymerization behavior was explored. When the addition of these groups was conducted incrementally, the groups were found to promote flexibility in the resulting linear polymer and to encourage formation of the polymer, whereas bulkier substituents inhibited polymer formation such that cyclic hexamers were the preferred product. Those catalysts found to be effective included both hexachlorocyclotriphosphazene and BCl_3 .

The introduction of ring strain as an aid to ROP was further supported by the attachment of diols to yield spirocyclic phosphazenes [56]. In these studies, 2,2'-bisphenol, 1,8-dihydroxynaphthalene, 1,8-diaminonaphthalene and catechol were found to readily attach in a geminal fashion (1,1-disubstituted) and, followed by treatment with sodium 2,2,2-trifluoroethoxide to remove remaining halide, yielded a stable trimer material (Figure 4.6). Additional structures formed exhibited 1,3 substitutions of selected bifunctional pendant groups, similar to that of the metallocenyl derivatives (Figure 4.7).

Studies into the polymerization of these trimers were conducted as a direct comparison to the polymerization chemistry observed for the metallocenyl derivatives. Both, the 2,2'-bisphenol 1,1 and 1,3-disubstituted trimers were found to be stable up to 200°C, and exhibited no decomposition or polymerization. However, at 200°C both trimers were found to undergo ring expansion to higher-order oligomers, with a high polymer being detected only in those samples provided with a catalytic amount of hexachlorocyclotriphosphazene. The more sterically rigid 1,3-disubstituted 1,8-dihydroxynaphthalene variant was found to produce polymeric products, both with and without catalyst, at 200°C, although significant ring expansion was also observed. Likewise, the catechol-substituted trimer was completely consumed, yielding polymer and oligomers at 250°C without a need for the hexachlorocyclotriphosphazene catalyst. Additionally, the 1,3-disubstituted

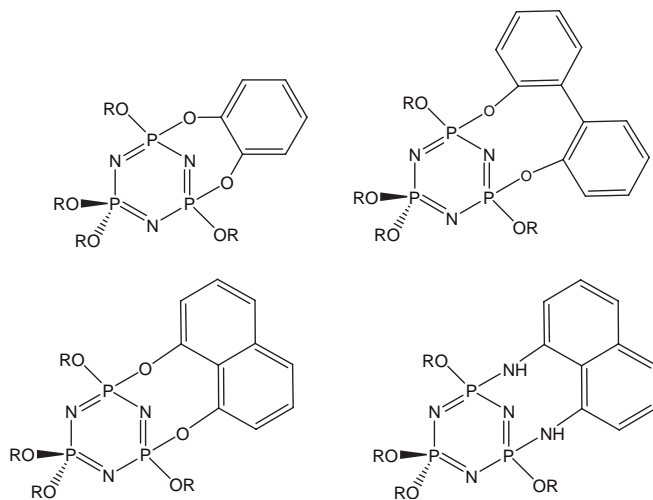


Figure 4.7 Various 1,3-disubstituted phosphazene trimers ($R = -CH_2CF_3$).

1,8-diaminonaphthalene trimer also formed polymer (albeit of a comparatively low molecular weight) and oligomers, with and without catalyst, at 200 °C.

The activity of organocyclotriphosphazenes towards ring expansion and linear polymerization appears to be a function of the degree of ring strain induced by the attachment of a bifunctional pendant group, which is a steric effect. A general pattern of behavior has been established where groups with specific characteristics must be added to the trimer/tetramer ring to induce ring-opening. However, as a preparative methodology for general linear polyphosphazenes, the preferred route is to form the polymer backbone in high molecular weight using halogenated rings by thermolysis under vacuum, at a temperature of least 250 °C, over a period of between 12 h and 12 days, depending on the purity of the trimer. In order to speed up the reaction, Lewis acid catalysts have been found to produce high polymers with significantly lower reaction times. Unfortunately, the reproducibility of the ROP process for polyphosphazenes remains much less controllable than other polymerization processes, and much of the actual chemistry that occurs is subject to further debate.

A significant (and more recent) finding was that trimers substituted with pyridinoxy pendant groups will undergo ROP to yield high polymers, in the absence of a catalyst, at a relatively low temperature [57]. The pyridinoxy trimers were synthesized simply from the pendant group sodium salt, with the pyridinyl nitrogen being placed at the 2, 3 and 4 positions (Figure 4.8), using 2-hydroxypyridine, 3-hydroxypyridine and 4-hydroxypyridine, respectively. The purified trimers were polymerized neat; however, studies to conduct the ROP in solution failed to produce high polymer.

Although ROP experiments were performed on all three trimers, only the 3-pyridinoxy trimer failed to polymerize at temperatures as high as 300 °C, even in the presence of hexachlorocyclotriphosphazene, $AlCl_3$ or water as catalyst. The

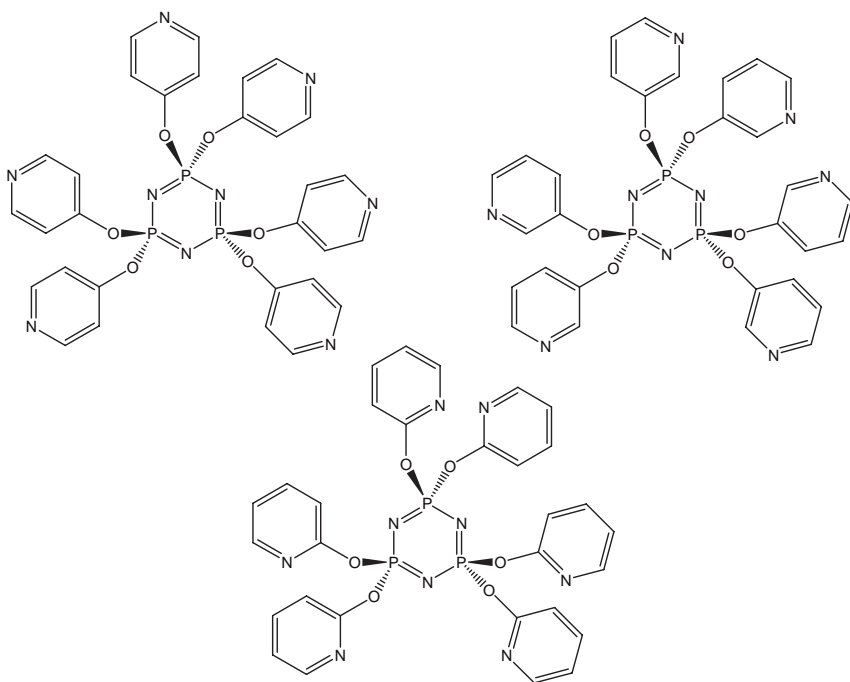


Figure 4.8 Cyclotriphosphazenes substituted with 4-hydroxypyridine (top left), 3-hydroxypyridine (top right) and 2-hydroxypyridine (bottom).

2- and 4-pyridinoxy trimers readily polymerized at temperatures above 200°C and 150°C, respectively. Considering the fact that these three trimers have near-identical steric bulk—as was invoked as an ROP influence in earlier studies—this was a surprising result. Clearly, this is an electronic effect where the lone electron pair on nitrogen provides an electron density on phosphorus to stabilize the cation formed by the initial loss of chloride. In order for this donation to occur, the nitrogen must be either *ortho* or *para* (2 or 4 position) to the phosphorus-bound oxygen. This result has an even greater significance in that it strongly supports the cationic mechanism for ROP of small phosphazene rings.

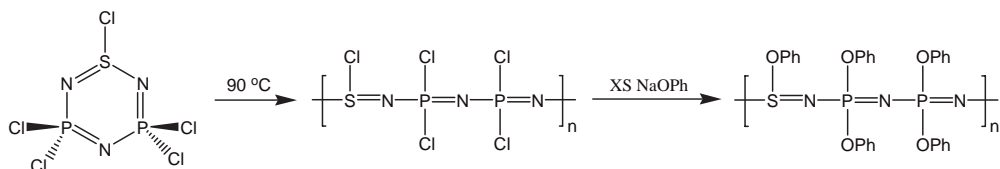
4.4

Incorporation of Sulfur into Phosphazene Ring Systems, and Their Polymerization Chemistry

4.4.1

Thiophosphazenes

The incorporation of other atoms besides phosphorus and nitrogen offers the possibility of creating new materials with differing chemistries and properties. The



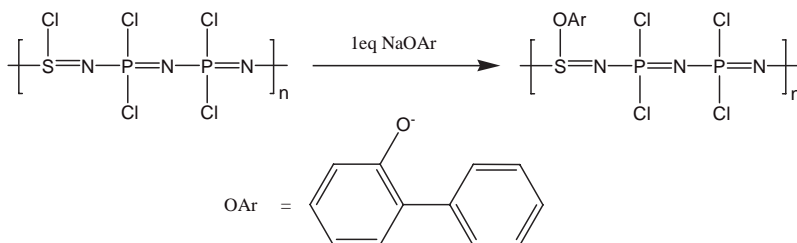
Scheme 4.14 ROP of thiatriazaphosphorine.

majority of heteroatom research performed to date has involved the incorporation of sulfur, with the initial report of ROP in sulfur-containing phosphazene rings having been published in 1990 [20] and including a discussion of the chemistry of a thiophosphazene six-membered ring (Scheme 4.14). Unlike hexachlorocyclo-triphosphazene, thiocyclophosphazenes are not commercially available; however, the six-membered variant, thiatriazaphosphorine, may be synthesized and isolated as an air- and water-sensitive oil, using published procedures [20, 58, 59].

The ROP of thiatriazaphosphorine was conducted neat in an evacuated Pyrex tube at 90 °C for 4 h, at which time a noticeable increase in viscosity was apparent. As with phosphazenes, the resulting high polymer was hydrolytically unstable and subsequently substituted with phenoxide by treatment with excess sodium phenoxide (Scheme 4.14). However, unlike phosphazenes, the resultant poly(thiophosphazene) was also unstable to moisture and exhibited degradation after being exposed for a few hours to wet solvents. Decomposition was proposed to be due to hydrolytic attack at the sulfur–nitrogen double bonds. An additional protection of the backbone was sought by replacing the backbone chlorine atoms with 4-phenylphenoxide, which is sterically bulkier than phenoxide. The ^{31}P NMR spectrum of this product polymer showed two peaks (rather than the expected single peak), which suggested an incomplete replacement of chlorine. Moreover, an elemental analysis revealed that approximately 65% of the chlorine atoms had been replaced.

With the product polymer containing both S–Cl and P–Cl bonds, a study of the relative reactivity of these two moieties can be examined. By limiting the amount of nucleophile to 1 equivalent per ‘S–P–P’ unit, the S–Cl bond was determined to be more susceptible to replacement than the P–Cl bond. Reaction of the polymer with 1 equivalent of sodium 2-phenylphenoxide yielded one product structure, with replacement only observed at S (Scheme 4.15).

A later report explored the substitution chemistry further [60], whereby a comparison was made between the previously published 2-phenylphenoxide, 3-phenylphenoxide and 4-phenylphenoxide. Moving the phenyl ring substituent further from the backbone lowered the steric bulk proximate to the backbone, thus leading to higher degrees of substitution. Reaction with excess 3-phenylphenoxide left approximately 11% of the chlorine atoms undisplaced, while the 4-phenylphenoxide-substituted polymer had 6% of the chlorines undisplaced. It should be noted that the 4-phenylphenoxide-substituted polymer also was more hydrolytically unstable, which suggested that pendant group protection of the backbone might be critical to polymer stability.



Scheme 4.15 Selective replacement of chlorine in polymerized thiatriazaphosphorine.

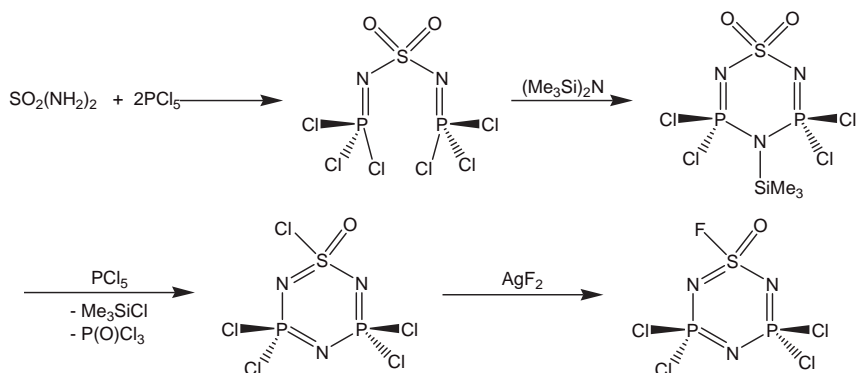
Samples of thiatriazaphosphorine that were sealed in ampoules *in vacuo* and stored at room temperature were found to increase in viscosity over a period of several weeks [60]. The material became elastomeric and was not soluble in 1,4-dioxane, and suggested that room temperature ROP followed by crosslinking had occurred. In a second experiment, a sample was prepared and slowly agitated by rocking. Under these conditions, a significant increase in viscosity was observed after four days, suggesting the onset of ROP. Stabilization of the product by substitution with 3-phenylphenoxide yielded a lower molecular weight polymer than was obtained through the 90 °C polymerization. Thus, although the thiophosphazenes were active towards ROP, the stability of the derived products was somewhat lower than that of phosphazenes, presumably due to the S(IV) centers incorporated into the backbone.

4.4.2

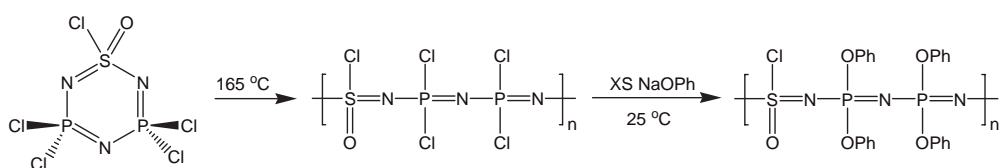
Thionylphosphazenes

Thionylphosphazenes are systems built upon S(VI), and the basic six-membered ring has been synthesized by vacuum thermolysis and a 3 + 3 cyclocondensation routes, although with low overall yields [61, 62]. A better route has the ring synthesized from a phosphazo-sulfone, which itself is synthesized from PCl_5 and sulfamide, in a 5 + 1 cyclocondensation with hexamethyldisilazane followed by conversion of the sulfone to the thionylphosphazene through reaction with additional PCl_5 (Scheme 4.16) [63]. Reaction with AgF_2 yields selective replacement of Cl for F on the sulfur only, demonstrating some interesting regiospecificity [64]. The advantage of the S(VI)-containing ring systems is that they are less susceptible to hydrolysis, as compared to the S(IV) analogue [65].

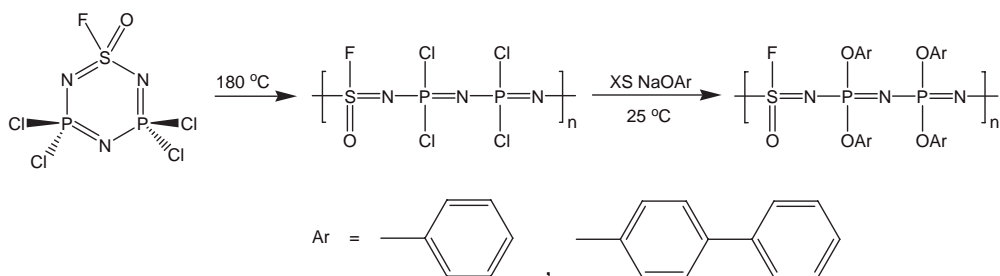
A successful ROP of cyclothionylphosphazene was conducted in an evacuated and sealed Pyrex tube at 165 °C for 4 h, yielding a linear polymer in an approximate yield of 80%, with the remaining material consisting of unreacted starting material (Scheme 4.17) [66]. Isolation of the polymeric material was accomplished by precipitation into hexanes from CH_2Cl_2 solution to yield a water-sensitive elastomer. Stabilization of this polymer was performed by reaction with excess sodium phenoxide at 25 °C in 1,4-dioxane. However, ^{31}P and ^{13}C NMR experiments, as well as elemental analysis, have shown that chlorine atoms bound to phosphorus were completely substituted, while chlorine remained on sulfur. This is a clear change



Scheme 4.16 Condensation route to the six-membered ring cyclothionylphosphazene.



Scheme 4.17 ROP of cyclothionylphosphazene followed by substitution with phenoxide.

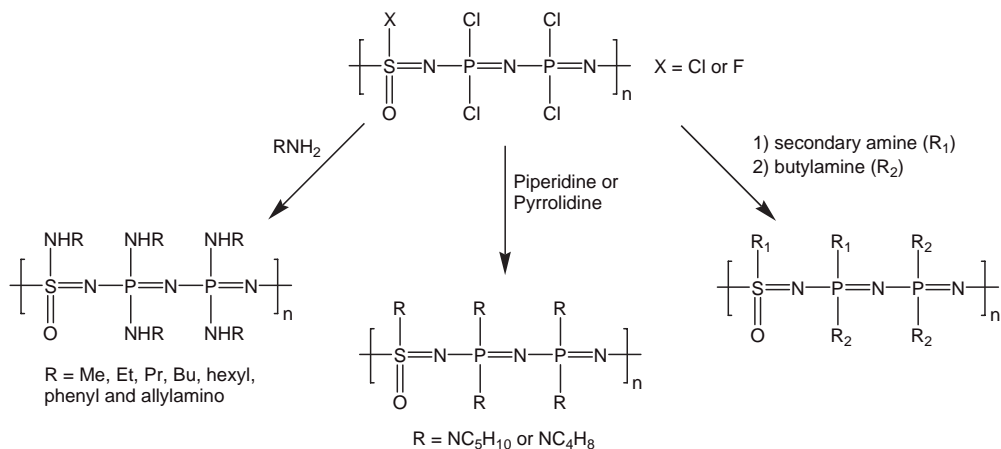


Scheme 4.18 Synthesis of fluorinated poly[(aryloxy)thionylphosphazenes].

in reactivity from the S(IV) systems in which the S–Cl bond was more labile than the P–Cl.

Another critical difference in reactivity was the observed hydrolytic stability. The substituted S(IV) polymers were not stable in water, presumably due to hydrolysis at sulfur. S(VI), on the other hand, does not provide access and ease of hydrolysis. Thus, the resulting aryloxy polymers are completely stable in the presence of water.

ROP of the fluorinated cyclothionylphosphazene was found to occur under the same conditions as the chlorinated analogue, although at a slightly higher temperature of 180 °C [67]. Stabilization of the polymer with organic nucleophiles obtained a stable hydrolytically stable polymer with fluorine substituted at sulfur atom (Scheme 4.18). Poly[(phenoxy)thionylphosphazene] was obtained in good yield



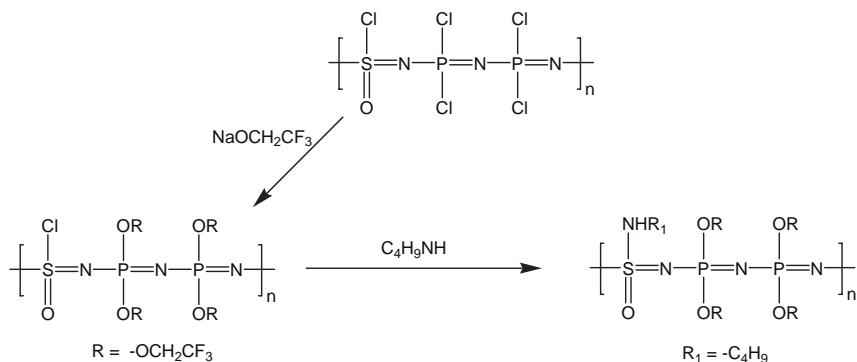
Scheme 4.19 Attachment of amino groups to thionylphosphazene.

as a white gummy elastomer, while poly[(4-phenylphenoxy)thionylphosphazene] was a white powder with a higher glass transition temperature (-15°C versus 48°C), which is induced by the steric bulk of the pendant groups.

The diversity of the chemistry of poly(thionylphosphazenes) was demonstrated through a series of reports [67–71]. In this series, poly(thionylphosphazenes) were observed to enjoy much of the chemistry of poly(phosphazenes), in that they could be substituted after polymerization with a variety of organic nucleophiles to yield materials with varying properties. Amino substituents were found to differ from the aryloxides in that substitution also was observed at sulfur (Scheme 4.19). Reaction with primary amines yielded polymers with all chlorine atoms replaced [69]. The reactions were conducted over 12–48 h at temperatures between 0°C and 25°C , and were monitored using ^{31}P NMR spectroscopy. Later studies extended this research to cyclic secondary amines, including piperidine and pyrrolidine [70]. Such studies also led into mixed substituent materials in which two differing pendant groups are attached to the same polymer backbone. In this instance, diethylamine, piperidine or pyrrolidine were first attached, followed by butylamine, which is a primary amine that would be expected to assure replacement of all chlorine atoms. The percentages of dialkylamine pendant groups ranged between 35 and 65%, while substitution was found to be random over S and P.

An interesting report indicated that regiospecific control was possible by using both oxygen- and nitrogen-containing nucleophiles [68]. An initial substitution of the poly(thionylphosphazene) with sodium trifluoroethoxide in 1,4-dioxane at 50°C was found to substitute all P–Cl moieties, leaving the S–Cl linkage intact. Subsequent treatment at 0°C with an amine yielded a mixed amino/alkoxy polymer with regiospecific pendant group placement (Scheme 4.20).

Further analysis of the byproducts from the ROP of the chlorinated cyclothionylphosphazene revealed macrocyclic structures, indicating that the ring expansion had occurred under thermal conditions [72]. Predominant in the dimer



Scheme 4.20 Regiospecific substitution of poly(thionylphosphazene).

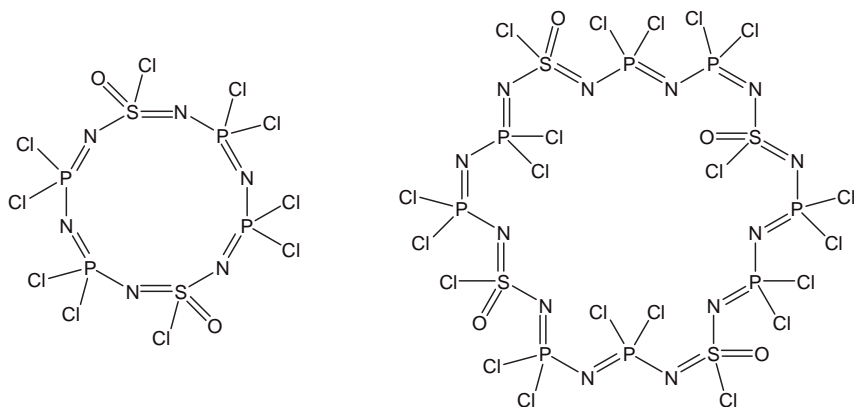
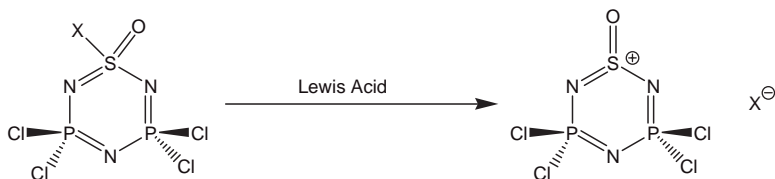


Figure 4.9 Ring expansion 12- and 24-member ring products of cyclothionylphosphazene.

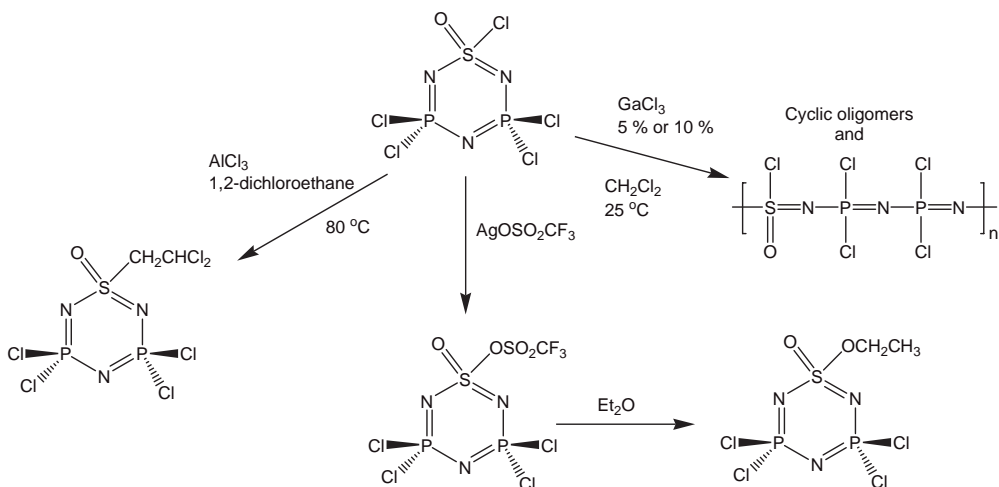
structure (Figure 4.9), however, were 24-membered rings, which suggested that the ring expansion may occur from both the six- and 12-membered rings.

Using the phosphazene studies as a basis of thought for the mechanism of thionylphosphazene ROP, a cationic intermediate has been proposed as the initial step in the polymerization (Scheme 4.21) [73]. As a test for this hypothesis, cyclothionylphosphazene was reacted with various Lewis acids including AlCl_3 , AgBF_4 , silver triflate and GaCl_3 ; however, no cationic products were isolated.

The AlCl_3 experiment was performed in 1,2-dichloroethane to avoid any Friedel–Craft-type chemistry between the trimer ring and a more commonly employed aromatic solvent. In this reaction, the product was identified as a solvent adduct with chloride migration, although the authors did not describe a mechanism (Scheme 4.22). Reaction with AgBF_4 yielded an AgCl precipitate, the fluorinated cyclothionylphosphazene, and presumably BF_3 as a gas. Reaction with silver triflate resulted in an addition of the triflate anion to sulfur, as well as some elastomeric residues with ^{31}P NMR signals consistent with polymer formation, suggesting that ROP had occurred. Exposure of the triflate adduct to diethyl ether



Scheme 4.21 Cationic intermediate proposed to be the initial step in the ROP of thionylphosphazenes.



Scheme 4.22 Reaction of cyclothionylphosphazene with various Lewis acids.

resulted in an ethoxy adduct, liberating EtOSO₂CF₃, implying that the triflate anion was weakly bound to the ring.

Reactions with GaCl₃ were found not to yield cyclic adducts, as had the other catalysts. Products from the use of 5% and 10% GaCl₃ at 25 °C yielded cyclic oligomers and linear polymer. This is a significant finding for two reasons: (i) it was the lowest temperature observed for ROP of phosphazene-type systems; and (ii) it represents a pathway that involves a reactive intermediate that leads to ROP, although the exact species was not isolated. It cannot be said that any of the adduct products necessarily led to ROP.

4.5

Summary and Prospects

Many studies have been performed to elucidate the ROP chemistry and mechanism in phosphazene-type ring systems with, in general, the bulk of the evidence strongly suggesting a cationic ROP mechanism in which a reactive intermediate is formed through the loss of halide. Attempts to isolate and characterize ROP

intermediates have been largely unsuccessful. However, the diversity of the chemistry for these types of ring system continues to grow. Cyclotriphosphazenes are the most-studied material, and thus we know far more about their chemistries. The newer sulfur-containing systems are intriguing because of their strong similarities in substitution chemistry with the phosphazenes, and also because of their differences. S(IV) rings undergo ROP to yield polymers where the S–Cl bond is more labile and exhibits preferential substitution. However, the S(VI) rings also readily undergo ROP, but the S–Cl bond is far more robust and will not substitute with oxo-nucleophiles. Further, the S(IV) polymers remain hydrolytically unstable, even when completely substituted with organics, while the S(VI) analogue is far more robust. Thus, within this class of P–S–N cycles as defined by the phosphazenes, thiophosphazenes and thionylphosphazenes as both cyclics and polymers, there are major differences that yield diverse material properties. However, there are strong parallels between the various systems in their chemistries and, most importantly, in the elusiveness of the proposed cationic ROP intermediate.

Acknowledgments

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5

Polymerization of Cyclic Depsipeptides, Ureas and Urethanes

Pieter J. Dijkstra

5.1

Introduction

The successful synthesis of poly(lactide) and poly(glycolide) and their copolymers through ring-opening polymerization (ROP) of the corresponding lactones—that is, lactide and glycolide (see Chapters 10 and 11)—triggered various research groups to study the preparation and ROP of cycles containing other heteroatoms. Aliphatic polyamides possess good thermal stability and mechanical properties compared to their polyester analogues, whereas aliphatic polyesters are interesting materials that are known for their inherent biodegradation. The rationale for research in the field of poly(ester amide)s is thus related to a combination of these properties, biodegradability, and good material and processing properties. These materials are particularly interesting for use in the biomedical field, or as degradable materials for environmental applications.

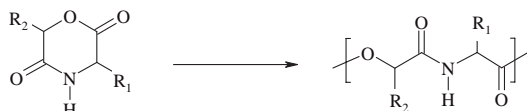
5.2

Polydepsipeptides

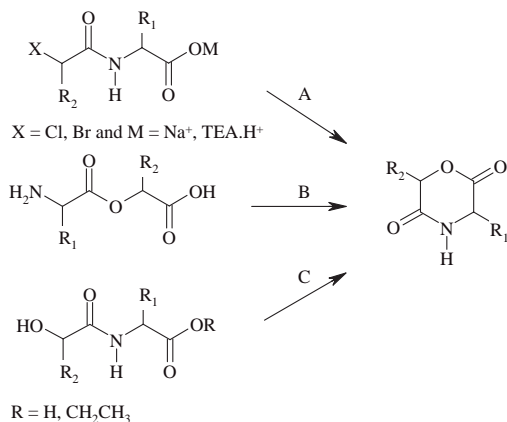
The majority of poly(ester-amide)s are prepared by the polycondensation of dicarboxylic acids with diols and diamines or, for example, polymerization reactions in combination with amino acids, lactones and lactams. During recent decades, many polymers have been prepared, and the synthesis and properties of these materials have recently been reviewed [1].

Among poly(ester-amide)s, the polydepsipeptides are materials with alternating hydroxy acid and amino acid moieties, and have been recognized as a potentially valuable addition to materials for the biomedical and pharmaceutical fields [2]. Because polydepsipeptides are compounds composed of an alternating array of hydroxy- and amino acids, they may be prepared from 2,5-morpholinediones through ROP (Scheme 5.1).

Based on the large number of natural amino acids present, and also commercially available, a large number of cyclic monomers can be prepared. The



Scheme 5.1 Ring-opening polymerization of 2,5-morpholinediones to alternating polydepsipeptides.



Scheme 5.2 Synthetic pathways to 2,5-morpholinediones.

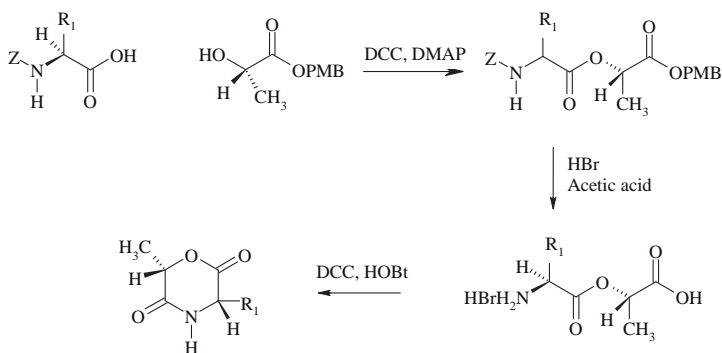
ring-opening homopolymerization of these 2,5-morpholinediones is expected to yield polymers with alternating amino acid and hydroxy acid units when the ring opening takes place exclusively through, for example, the ester functional group. Moreover, side-chain functional groups become available, although protection–deprotection steps will be necessary.

5.3

Monomers

During the past 20 years, a number of synthetic methods have been investigated systematically for the preparation of 2,5-morpholinediones as monomers in the production of polydepsipeptides through ROP. The synthesis of 2,5-morpholinediones through the cyclization of acylated amino acids or aminoacyl hydroxy acid derivatives has been accomplished as depicted in Scheme 5.2. In route A, the salts of *N*-(2-halogenacyl)-amino acids are cyclized by the formation of an ester bond, whereas in route B, activated aminoacyl hydroxy acids are cyclized by formation of an amide bond [3]. The (trans)esterification reaction (route C) was developed more recently as an alternative preparative tool [4].

The preparation of morpholine-2,5-diones derivatives via route A was first described by Chadwick and Pascu [5], who found that upon dry-heating *N*-[(2 *R,S*)-bromopropionyl]-glycine, (6 *R,S*)-methylmorpholine-2,5-diones was formed. This



Scheme 5.3 Synthesis of an optically pure (3*S*,6*S*)-3-isopropyl-6-methyl-2,5-morpholinedione. Z = benzyloxycarbonyl; PMB = pentamethylbenzyl. First step; *N,N'*-dicyclohexylcarbodiimide/4-dimethyl-aminopyridine (DCC/DMAP). Second step; HBr/Acetic acid. Third step; Triethylamine, *N,N'*-dicyclohexylcarbodiimide/1-hydroxybenzo-triazole (DCC/HOBT).

method has been used frequently to synthesize several 3- and 6-substituted morpholine-2,5-diones [6–11].

Only a few examples of 2,5-morpholinediones prepared via route B have been reported. Shemyakin *et al.* [12] prepared cyclic depsipeptides by cyclization of the acid chlorides of aminoacyl hydroxy acids, whereas Goodman and coworkers [13] found 2,5-morpholinediones to be the main products in the polymerization of trifluoroacetate salts of the aminoacyl hydroxy acids pentachlorophenyl esters.

These methods (routes A–C) have both their advantages and disadvantages. Route A has the advantage that the intermediate *N*-(2-halogenacyl)-amino acids can easily be prepared in one step by reacting amino acids with 2-halogenacyl halogenides. However, the yields of the 2,5-morpholinedione from the ring-closure reaction depend heavily on the amino acid and hydroxy acid used. In general, more highly substituted compounds tend to give higher yields. The cyclization reaction is performed in the solid state at temperatures of approximately 130–150 °C, and the cyclic depsipeptide is collected through sublimation. Besides formation of the 2,5-morpholinedione, oligomerization might also be observed. The yield of the monomer is improved by subjecting the remainder polymeric mixture to depolymerization with ring closure, and is achieved at higher temperatures using Sb₂O₃ as a catalyst. The cyclization reaction may also be performed in *N,N'*-dimethylformamide using triethylamine as a base. This method is frequently used to synthesize 3-substituted 2,5-morpholinediones [3].

The method represented by route B requires a multistep synthetic route employing synthetic techniques commonly used in peptide chemistry, and was only used to prepare enantiomerically pure 2,5-morpholinediones.

From the reaction depicted in Scheme 5.2, it can be seen that in the case of using a lactic acid derivative racemization will take place when the ring-closure reaction is performed via pathway A. Synthesizing the monomer via pathway B

Table 5.1 2,5-Morpholinediones with 3- and/or 6-alkyl substituents.

R ₁	R ₂	Route ^a	Yield ^b (%)	Melting point (°C)	α_D^{25c}	Reference(s)
H	H	A	13	193–194	–	[14, 15]
		A	16	192–193	–	
H	(RS)CH ₃	A	50	99–100	–	[3]
H	(S)CH ₃	C	50	161–163	–87	[4]
(S)CH ₃	H	A	5	154–156	–69	[3]
(S)CH ₃	(RS)CH ₃	A	83	129–137	–130	[3]
(S)CH ₃	(S)CH ₃	C	59	100–102	–161	[3, 4]
		A	28	162–163	–165	
(S)CH(CH ₃) ₂	H	C	29	96–97	36	[3, 4]
		A	4	96–97	37	
(S)CH(CH ₃) ₂	(RS)CH ₃	C	30	129–130	–52	[3, 16]
		A	23	110–125	–54	
(S)CH(CH ₃) ₂	(S)CH ₃	C	30	134–136	–129	[3, 4]
		B	13	136–137	–136	

a See Scheme 5.2.

b Yield of the cyclization reaction.

c α_D^{25} : Optical rotation (for solvents and concentrations, see references).

avoids racemization in the ring-closing step, such that optically pure 2,5-morpholinediones are synthesized.

Cyclization via route C circumvents racemization at the C-6 carbon atom, as will happen when cycles are prepared via route A. The esterification/transesterification reaction with ring closure represents a convenient method of synthesizing the 2,5-morpholinediones, although in some cases it is laborious and the yields of the cyclization reaction range from low to good. Although the ring-closing reaction is expected to proceed without racemization at the C-6 carbon atom, minor racemization on this carbon was observed in some cases, sometimes depending on the reaction conditions employed [4].

A large variety of 2,5-morpholinedione derivatives comprising either a glycolic or lactic acid as the α -hydroxy acid, and glycine, alanine, valine, leucine or isoleucine as the α -amino acid residue, have been synthesized via routes A and C. Details of some representative 2,5-morpholinediones with relevant physical data are summarized in Table 5.1.

5.4

Ring-Opening Polymerization

The parent cyclic depsipeptide is 2,5-morpholinedione, built from a glycolic acid and a glycine moiety [14]. This compound has a melting point of $\sim 200^\circ\text{C}$, and is

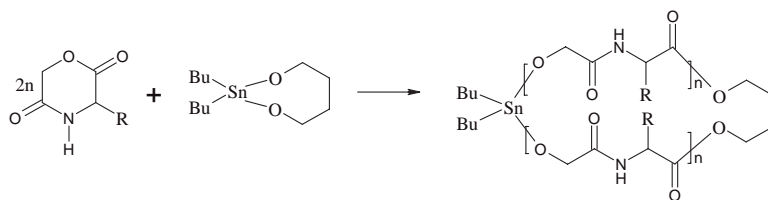
only slightly soluble in common organic solvents. ROP in the bulk (i.e. in the absence of solvent) using stannous octanoate as a catalyst, which is successfully used in the ROP of lactide and other lactones (see Chapters 10 and 11), is only possible when the temperature is maintained just below the melting temperature. Decomposition and interchange reactions apparently hamper the homopolymerization of this high-melting monomer. Copolymerization with, for example, glycolide gives better results, and polymers with maximal molecular weights of $\sim 10\,000\text{ g mol}^{-1}$ can be prepared. Until now, the relationship between ring conformation and the polymerizability of these rings has not been studied in detail, although interestingly some recent studies have provided new insights. These studies relate to the crystal structure of 2,5-morpholinediones, complexes of these monomers with the catalyst metal center, and studies on the polymer structures obtained when using different types of catalyst.

The most stable conformation of cyclic depsipeptides appears to be a 'boat' or 'twist-boat' conformation [17, 18]. Hydrogen bond formation in the twist-boat conformation may stabilize the 2,5-morpholinediones, and likely contributes to ring stability. This has been attributed to the high *trans-cis* barrier for the nonalkylated amide bond. In order to form the cyclic compounds, the linear precursors should adopt a folded conformation with a *cis* amide bond, rather than the more extended and favored *trans* amide bond. Thus, rather drastic conditions are required for the formation of 2,5-morpholinedione derivatives [19].

The mechanism of the bulk ROP of 2,5-morpholinediones using a catalyst such as stannous octanoate takes place similar to that of lactones, such as lactide and caprolactone. The ring opens at the ester bond with water (or, if present, an alcohol) as the initiator. Despite the numerous catalysts developed for the ROP of lactides and other lactones in the preparation of aliphatic polyesters, very few have been tested for the ROP of 2,5-morpholinediones. In many cases, the catalyst of choice remains stannous octanoate. In general, moderate to good yields of polymers are obtained, although a full monomer conversion can hardly be reached. It has been reported that, at high monomer conversion, side reactions take place and the molecular weights actually decrease. In a comparative study, polymerization appears to be better controlled when using a catalyst such as tin acetylacetonate [20]. It is worthy of mention at this point that, in most cases, racemization during polymerization seems to take place at the hydroxy acid unit.

Ring-expansion polymerization—which is also known as macrocyclic polymerization (as developed by Kricheldorf and Hauser [15])—uses initiators such as 2,2-dibutyl-2-stanna-1,3-dioxepan (DSDOP) (see Scheme 5.4).

This cyclic initiator allows controlled polymerization, and is used to prepare a variety of polymeric architectures ranging from block copolymers to polymeric networks. The ROP of D,L-3-methyl-2,5-morpholinedione and 2,5-morpholinedione with DSDOP at a monomer-to-initiator (M/I) ratio of 1000 at 130 °C for 16 h gives somewhat higher polymer yields and molecular weights as compared to stannous octanoate. However, it has been found that full control over the molecular weight via the M/I molar ratio is not possible. In addition, no reaction is observed when the polymerization is conducted with this initiator in solution



Scheme 5.4 Ring-expansion polymerization of 2,5-morpholinediones ($R = H, CH_3$) with 2,2-dibutyl-2-stanna-1,3-dioxepane (DSDOP) as an initiator.

at 80°C. The oxybutane unit appears not present, which leads to the conclusion that ring-expansion polymerization does not in fact take place.

Recently, Castro *et al.* [21] studied a single-site yttrium alkoxide initiator (an alkoxyamino-bis(phenolate) yttrium alkoxide complex) in the ROP of (3*S*,6*S*)-dimethyl-2,5-morpholinedione. In the ROP of lactones such as lactide and caprolactone, lanthanide catalysts represent highly active catalyst systems, especially when they are formed *in situ* from sterically blocked precursors. Solution polymerization in toluene revealed that the alkoxide catalyst/initiator promotes the ROP of 2,5-morpholinediones. Side reactions such as transesterification, the formation of cyclic oligomers and intramolecular transamidation were detected using MALDI-ToF mass spectrometry experiments, and depended on the reaction temperature applied. Finally, Chisholm *et al.* [18] systematically investigated the use of different organotin compounds in the ring-opening of 2,5-morpholinediones. Tin alkoxides appeared ineffective in these ROPs because of coordination of the 2,5-morpholinedione to the metal complex via the amide functional group and side reactions leading to kinetically inert compounds. Consecutively, this leads to complexes that are inert to further ring opening of the 2,5-morpholinediones. These experiments all pointed to several possible interchange reactions, such as transesterification and transamidation, which occur readily at higher temperatures in both bulk and solution. Moreover, the regularly observed racemization of the hydroxy acid unit hampers the synthesis of stereoregular polymers. Especially, chiral polydepsipeptides prepared from, for example, (3*S*,6*S*)-3,6-dimethyl-2,5-morpholinedione, are interesting with regards to the possible formation of stereo-complexes with its *R*-enantiomer, as observed for poly(lactides). A possibility of the formation of cyclic oligodepsipeptides from 2,5-morpholinediones has also recently been demonstrated [22]. These types of compound have biological activity, a well-known example being valinomycin, a macrocyclic depsipeptide that selectively complexes potassium ions.

Anionic polymerization using potassium alkoxides has also been applied in the ROP of the 2,5-morpholinediones to provide polymers with a narrow molecular weight distribution [23].

Polydepsipeptides with *N*-alkyl-substituted α -amino acid residues, such as poly(*N*-methylglycine-alt-*D,L*-lactic acid) and poly(*N*-isopropylglycine-alt-*D,L*-lactic acid), cannot be polymerized by a ring-opening reaction from the corresponding *N*-alkyl-substituted 2,5-morpholinediones [24].

The use of trifunctional amino acids, such as lysine, glutamic or aspartic acid, cysteine and serine, in the synthesis of 2,5-morpholinediones, allows the introduction of respectively amine, carboxyl, thiol and hydroxyl functional groups [25–40]. In the synthesis of the cyclic depsipeptide, the functional group must be protected, and most commonly benzyloxy or benzyl groups are used for this purpose. These groups can be completely removed after ROP by catalytic hydrogenation or by an acid treatment of the polydepsipeptide. Monomers containing a lactic acid moiety are much less reactive in ROP than the corresponding monomers, which are unsubstituted at the 6-position (glycolic acid derivatives). Cyclization of the *N*-(2-halogenacyl)-amino acid intermediates has been performed with triethylamine (TEA) or NaHCO_3 , albeit with generally low yields.

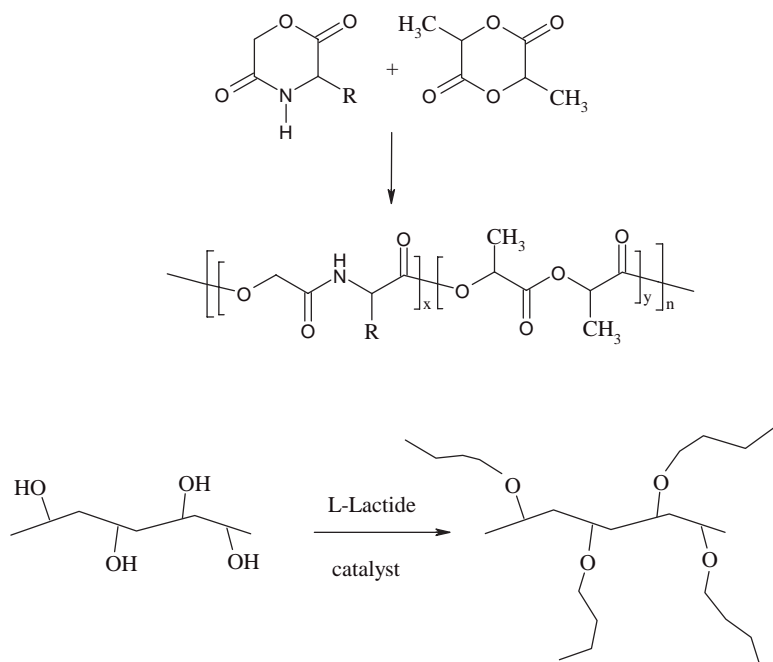
The 2,5-morpholinedione derivatives that have functional protected groups at the 3-position but are unsubstituted at the 6-position, can be homopolymerized, but with only low to moderate yields. Copolymerization with lactide, glycolide or ϵ -caprolactone allows a variation of the number of pendant functional groups; diblock copolymers are readily available by sequential polymerization of lactide and 2,5-morpholinedione derivatives. The initiation of lactide polymerization by 2,5-morpholinedione-based macroinitiators has been reported by Ouchi *et al.*, as depicted in Scheme 5.5 [41].

At this point, some alternative methods are worthy of mention for the synthesis of polydepsipeptides. The copolymerization of lactones and amino acid carboxyanhydrides using stannous octanoate as catalyst affords random polydepsipeptides, and is an attractive way to prepare polymers with pendant functional groups [42]. In addition, the ROP of amino acid *N*-carboxyanhydrides and lactic acid anhydrosulfite affords polymers the structure of which may be either random or 'blocky-like', depending on the catalyst/initiator system used [43, 44].

In the stannous octanoate-catalyzed ROP of 2,5-morpholinediones, alcohols are frequently used as initiators. When using hydroxyl telechelic poly(ethylene glycol) (PEG), the ROP affords block copolymers in good yields with molecular weight distributions ranging from 1.35 to 1.83. The molecular weight of the depsipeptide blocks appears to be lower than the values expected from the feed ratio, but all hydroxyl groups do react and pure triblock copolymers are readily obtained. Similarly, the incorporation of carboxylic acid functional groups into the side chain of the B-blocks produces amphiphilic materials, using procedures as described above for the ROP of glutamic acid-based 2,5-morpholinediones.

The ROP of 3-methyl-2,5-morpholinedione can also be achieved successfully by applying amino telechelic PEG as the initiator; in this case, a catalyst is not necessary [45–48].

Based on the results of the studies presented so far, it can be concluded that 2,5-morpholinedione derivatives comprising a glycolic acid moiety are more reactive than those with a lactic acid moiety. The reactivity of 3- and/or 6-alkyl-substituted 2,5-morpholinedione derivatives decreases with increasing number and size of the alkyl substituents under the same reaction conditions. This decrease can be attributed to an increase in steric hindrance and stability of the ring structure. The low reactivity of 2,5-morpholinedione derivatives can be attributed to an



Scheme 5.5 Comb-type poly(lactide) by graft polymerization of lactide onto a poly(glycolic acid-serine-r-lactide) copolymer. In the copolymerization of the 2,5-morpholinedione with lactide, the R-group is a benzyl-protected CH_2OH group that is deprotected with trifluoromethanesulfonic acid and thianisole/trifluoroacetic acid to give the hydroxyl functionalized macroinitiator.

interaction of the catalyst with the amide bond of the ring. The introduction of a substituent carrying a protected functional group in the 2,5-morpholinedione derivatives may also result in a reduction in reactivity, caused by an interaction between the catalyst and the pendant functional group. Although the results published to date are difficult to compare (due to differences in reaction conditions), it seems that that reactivity of the cyclic depsipeptide carrying a protected functional group decreases in the following order: glutamic acid > aspartic acid > serine > lysine.

5.5

Enzymatic Polymerization

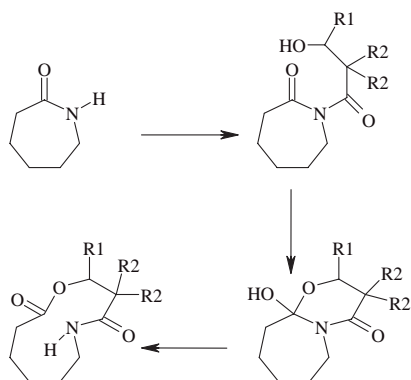
The first report of an enzymatic ROP of 2,5-morpholinediones appeared in 1999, when Höcker, Feng and colleagues showed that alternating polydepsipeptides could be prepared from 2,5-morpholinediones with different alkyl substituents (methyl, isopropyl, *sec*-butyl) at the 3- or 6-position, and using different enzymes,

including porcine pancreatic lipase (PPL), *Pseudomonas* sp. and *Candida rugosa* as catalysts [16, 49, 50]. The ring opening takes place at the ester bond, with high conversions being reached at temperatures up to 130°C. Polymers with carboxylic acid and hydroxyl end groups were obtained and characterized by molecular weights which generally ranged between 10 000 and 20 000 g mol⁻¹, together with narrow molecular weight distributions. Increasing the water content was found to lead to higher rates and lower molecular weights. As steric effects were also shown to play a role when the ring opening took place exclusively at the ester bond, the conversion of monomers carrying a methyl substituent at the 6-position (lactic acid derivatives) proved to be much lower. The polymerization of 2,5-morpholinediones with an isopropyl group at the 3-position (valine moiety) having different optical configurations (*S*, *R* or *R,S*), gave materials with much lower optical rotations compared to those prepared via stannous octanoate-catalyzed ROP. Moreover, the racemization of 6(*S*)-methyl-2,5-morpholinedione was also observed during polymerization using PPL, and provided evidence that *R,S*-amino acids and *S*-lactic acid residues were easily racemized in the PPL-catalyzed ROP of 3 and/or 6-substituted 2,5-morpholinediones.

5.6 Ring Expansion

Larger rings containing an ester and amide functional group are potential monomers that can be used for the synthesis of poly(ester-amide)s through ROP. Shemyakin *et al.* [51] have prepared such rings by a ring expansion reaction of *N*-acyl-lactams (Scheme 5.6). A detailed study on the applicability of this reaction, the development of alternative pathways and the ROP for the synthesis of poly(ester-amide)s was studied in detail by Robertz *et al.* [52–55].

These authors successfully prepared 11- and 14-membered cycloesteramides by the ring-expansion of *N*-(hydroxyacyl)-lactams and *N*-(hydroxyacyl)-2,5-diketopiperazines. The mechanism involved a nucleophilic attack of the hydroxyl

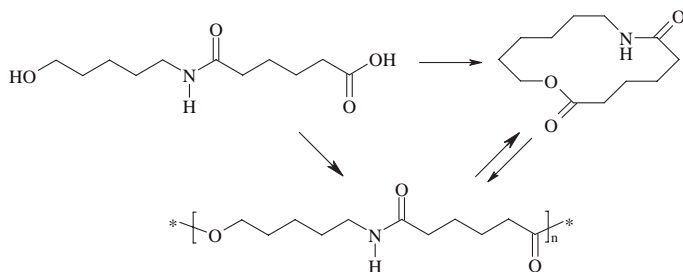


Scheme 5.6 Ring expansion of acyl-lactams [52].

group ($X = OH$) on the carbonyl C atom, with the formation of a bicyclic compound that isomerized to the cycloester-amide. The course of the reaction was seen to depend on the steric accessibility of the amide carbon atom, the ring size of the lactam, the ring formed, and the nucleophilicity of the hydroxyl group. The yield of the cyclic ester-amide by ring expansion of the acyl lactam was moderate. When $R_2 = CH_3$ and $R_1 = H$, a good yield of the cyclic ester-amide was obtained [52].

The ROP of the monomers has been studied in detail, and showed that substituents in the 11-membered cycloester-amides have a large influence on the reactivity of these monomers. The unsubstituted monomer ($R_1 = R_2 = H$, melting point $142^\circ C$) gives mainly oligomers in the ROP conducted in the melt using anionic, coordination or transesterification catalysts. The unsubstituted cycloester-amide can be polymerized with dibutyltin dimethoxide as a catalyst/initiator in N,N' -dimethylformamide ($10\,000 < M_n < 16\,000\text{ g mol}^{-1}$) to give a semicrystalline polymer with a T_m of $146^\circ C$ after 120 h at a polymerization temperature of $100^\circ C$. The polymer contained the expected methyl ester and hydroxyl end groups, based on a coordination–insertion mechanism. However, the observed ratio of end-groups in the NMR spectrum was different from that expected from the feed ratio, the difference being due to the formation of a cyclic ester-amide end-group. The monomer with $R_2 = CH_3$ and $R_1 = H$ (melting point $165^\circ C$) can undergo ROP in the melt at $170^\circ C$ with anionic, coordination or transesterification catalysts, with the polymers obtained having an alternating sequence of the amino- and hydroxy acid units; it also appeared that a cyclic polyester-amide was formed [53]. The mechanisms operating have been summarized in a report which also described the mechanistic aspects of the ROP of cyclic carbamates, ureas and carbonates [54]. Ring-expansion reactions were also performed with N,N' -bis(hydroxyacyl)-2,5-diketopiperazines. The 14-membered cycles prepared from 2,5-diketopiperazines were high melting solids and too stable to undergo ROP.

More recently, cyclic ester-amides were prepared from α -carboxyl- ω -hydroxyl amides through their corresponding polycondensates by ring-closing depolymerization. These compounds may be readily synthesized from adipic anhydride and amino alcohols [55–59]. ROP afforded semicrystalline materials with melting points that depended on the number of methylene groups in the amino alcohol unit (odd–even effect) and ranged from 100 to $150^\circ C$ (Scheme 5.7) [59].



Scheme 5.7 Interconversion of a α -carboxyl- ω -hydroxyl amide to a cyclic esteramide, and its polymerization [59].

The polymerization appeared to be controlled by using catalyst/initiators such as dibutyltin dimethoxide and titanium butoxide.

5.7

Polyureas

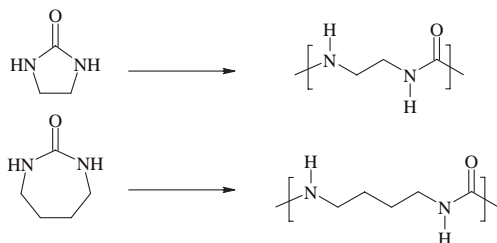
Although the method was proposed by Hall as far back as 1958 [60], the ROP of cyclic ureas has attracted only minor interest. The five- and seven-membered cyclic ureas (Scheme 5.8), which are referred to as dimethylene urea and tetramethylene urea, can be successfully ring-opening polymerized. Examples of suitable catalysts for dimethylene urea are sodium hydride, sodium hydroxide, *sec*-butyllithium, dibutylmagnesium and diethylzinc. The ROP of tetramethylene urea is achieved by heating in the melt or in solution in the presence of sodium hydride [60].

In earlier studies conducted by Höcker *et al.*, the copolymerization of trimethylene carbonate and caprolactam was shown to give a poly(ester-urethane). In a similar way, tetramethylene urea can be copolymerized, using dimethyltrimethylene carbonate and dibutylmagnesium as an initiator, to yield polyurethane chains [61, 62].

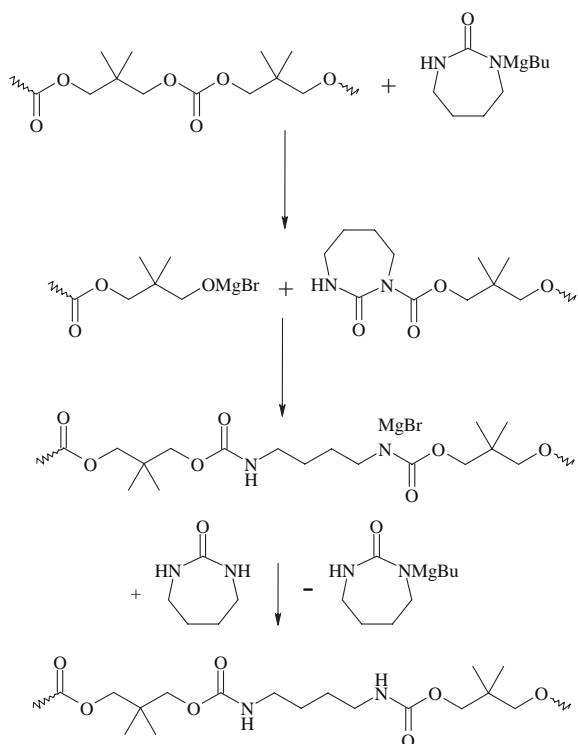
The mechanism of the copolymerization involves the reaction of an organomagnesium alcoholate of the polycarbonate (Scheme 5.9), the active site of which reacts with the cyclic urea to produce the organomagnesium salt of the cyclic urea. This salt then reacts with a carbonate bond of the polycarbonate to give an activated cyclic urea. Subsequently, ring opening occurs with the regeneration of an activated cyclic urea, and the reaction continues until all carbonate groups have been consumed.

This method used to prepare polyurethanes has been extended to the ring-opening copolymerization of cyclic ureas and ethylene carbonate (Scheme 5.10) [63]. Ethylene carbonate is an example of a monomer used in polymer syntheses that is not prepared from phosgene, but is readily available from ethylene oxide and carbon dioxide. The use of carbon dioxide for the preparation of polymers is an excellent option, from both an economical and—in particular—from an ecological point of view.

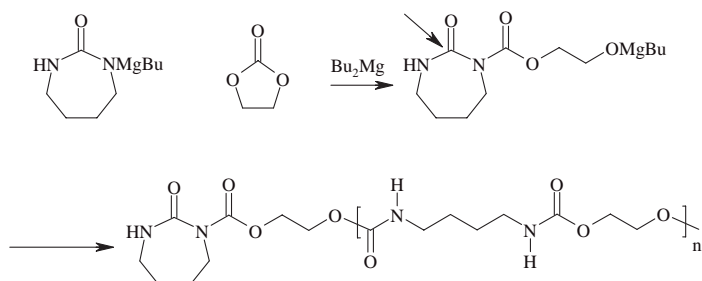
Dibutylmagnesium does not initiate the homopolymerization of tetramethylene urea or that of ethylene carbonate, and thus no homopolymer can be prepared with this initiator. Because dibutylmagnesium converts a mixture of the cyclic urea and



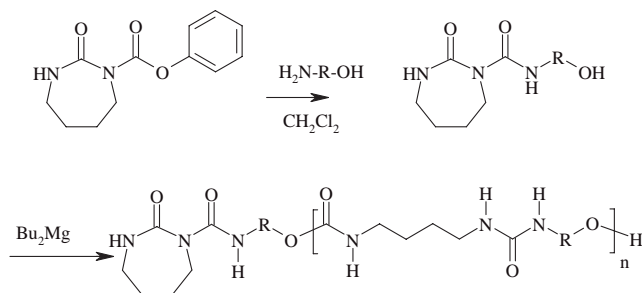
Scheme 5.8 Ring-opening polymerization of dimethylene urea and tetramethylene urea.



Scheme 5.9 Insertion reaction of an organomagnesium tetramethylene urea in a polycarbonate with the formation of two urethane groups.



Scheme 5.10 Mechanism of the reaction between tetramethylene urea and ethylene carbonate. The initially formed butylmagnesium alcoholate reacts with itself (indicated by the arrow) to give a polyurethane [63].



Scheme 5.11 Polyurethane ureas from ‘blocked isocyanates’.

A small amount of tetramethylene urea is formed during the polycondensation reaction.

the cyclic carbonate into an alternating copolyurethane, another mechanism seems to operate. In this mechanism (see Scheme 5.10) the magnesium salt of the cyclic urea reacts with the carbonate bond, after which the newly formed alcoholate reacts as a bifunctional monomer whereby the alcoholate oxygen adds nucleophilically to the endocyclic carbonyl carbon (as indicated by the arrow) [56].

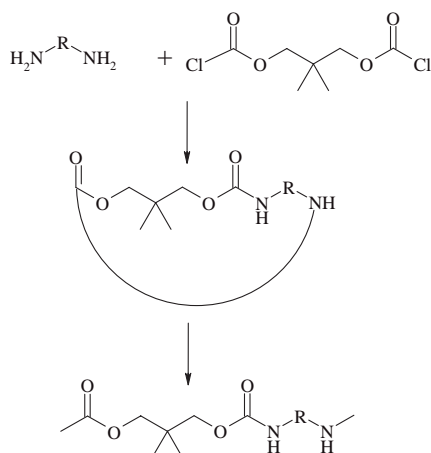
The elucidation of the mechanism of ring-opening copolymerization of cyclic urea and carbonates offered opportunities to study the general applicability of this mechanism to the copolymerization of tetramethylene urea with other monomers. The five-membered lactone, γ -butyrolactone, is a readily available and cheap monomer, which may barely be homopolymerized (see Chapter 11). The copolymerization of tetramethylene urea with γ -butyrolactone in the presence of dibutylmagnesium as catalyst in the melt at 100 °C resulted in an alternating poly(amide urethane) ($M_n = 12\,600\text{ g mol}^{-1}$; $M_w = 21\,000\text{ g mol}^{-1}$; $M_w/M_n = 1.67$) [64].

As mentioned above, dibutylmagnesium does not initiate the homopolymerization of tetramethylene urea or γ -butyrolactone under the reaction conditions applied. Rather, the ring opening proceeds in a similar manner as described for the copolymerization of dimethylene carbonate, and thus it allows the preparation of terpolymers. The reactivity of dimethylene carbonate is much higher than that of γ -butyrolactone and propylene oxide.

In the context of the above-mentioned N-substituted cyclic ureas, the concept of using blocked isocyanates was considered. Compounds such as phenyl-2-oxo-1,3-diazepane-1-carboxylate and ethyl-2-oxo-1,3-diazepane-1-carboxylate are blocked isocyanates, in which the O-phenyl urethane or O-ethyl urethane are considered as an activated urethane and the 1,3-diazepan-2-one ring as an intramolecularly blocked isocyanate (Scheme 5.11). The polymerization of such substituted ureas shows much promise [65].

5.8 Polyurethanes

New routes to polyurethanes are currently being investigated as attractive ways to circumvent the use of highly toxic isocyanates and phosgene in their preparation.



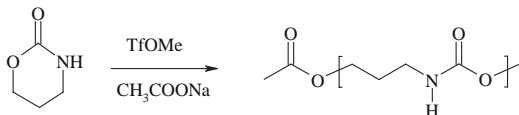
Scheme 5.12 Ring-opening polymerization of cyclic diurethanes prepared from diamines and 2,2-dimethyltrimethylene bis(chloroformate). Melt polymerizations were performed with, for example, titaniumisopropoxide or Sn(II)oct_2 . Solution polymerizations were performed with, for example, titaniumisopropoxide or $\text{Bu}_2\text{Sn(OMe)}_2$.

The broad applicability of polyurethanes in, for example, synthetic foams paints and adhesives is a driving force to explore these new routes of which the ROP of cyclic carbamates or the reaction of cyclic carbonates and amines are major strategies. This section has been purposely restricted to the ROP of cyclic carbamates; the polycondensation of diamines and cyclic carbonates is not included, but has been recently summarized elsewhere [66].

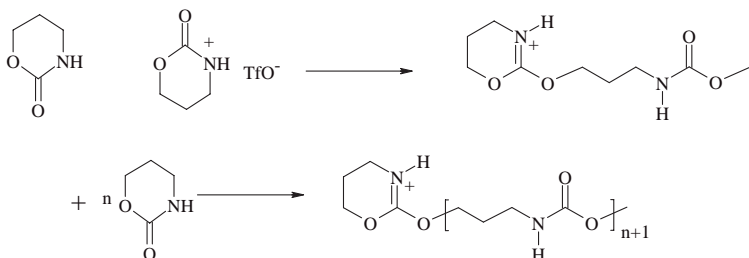
In the reaction of bis-chloroformates and diamines, cyclic diurethanes can be obtained under high-dilution conditions (Scheme 5.12). The ROP of cyclic diurethanes leads to polymers containing carbamate, urea and carbonate linkages, and showing that a variety of reactions takes place [67].

Although, in the past the ROP of cyclic carbamates has been rarely mentioned, it has been the subject of more detailed study more recently [56]. The six-membered trimethylene carbamate was the first cyclic carbamate to be successfully ring-opened by employing trifluoromethane sulfonate as the catalyst. Only the unsubstituted six- and seven-membered cyclic carbamates (Scheme 5.13) can be ring-opening polymerized [68–70]. The cationic ROP has subsequently been used in block copolymerizations starting from tetrahydrofuran (THF) to yield either AB- or ABA-type polymers.

The cationic ROP of trimethylene carbamate affords the corresponding polyurethanes with a regular microstructure [71–76]. The reaction is performed in the melt at 100°C , and high conversions/yields are obtained. The mechanism and kinetics of the polymerization reaction, when studied in detail, was shown to proceed via an active chain end with a protonated cyclic *endo* iminocarbonate as the active species and an absence of transfer reactions. In fact, the reaction involves



Scheme 5.13 Cationic ring-opening polymerization of a cyclic carbamate.



Scheme 5.14 Initiation and propagation of the trifluoromethane sulfonic acid-initiated polymerization of trimethylene carbamate.

alkyl oxygen cleavage, as depicted in Scheme 5.14. In this way, polymers with molecular weights up to 12000 g mol^{-1} and with controlled end-groups were prepared. Termination by the addition of acetate ions leads to heterobifunctional polyurethanes, which may be of interest in macromolecular engineering [75].

5.9

Summary and Prospects

The ROP and copolymerization of six-membered heterocyclic monomers comprising an ester and amide functional group affords poly(esteramides) with alternating hydroxy acid and amino acid residues. The use of amino acids as starting materials in the synthesis of these monomers is a straightforward method for preparing also polymers with pendant functional groups that can be used as starting points or anchoring points for a variety of modifications, such as polymerizations and coupling reactions with biologically active compounds. In general, due to bulkiness of the side chains, the reactivity of these cycles is generally lower than that of monomers such as lactide and glycolide in the ROP reaction.

The ROP of cyclic ureas has received scant attention, most likely because these types of material are more conveniently prepared via polycondensation reactions. However, cyclic ureas can be copolymerized with, for example, cyclic carbonates and lactones to afford a wide variety of new polymer architectures. The hydrogen-bonding ability of functional groups in these polymers may be highly profitable when designing materials with advanced properties. Routes to prepare polyurethanes through the ROP of cyclic urethanes have been investigated more recently as attractive ways to circumvent the use of the highly toxic compounds that

are commonly used for their synthesis. The broad applicability of polyurethanes represents a driving force for the exploration of new routes of which the ROP of cyclic carbamates, or the reaction of cyclic carbonates and amines, are major strategies.

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6

Polyethers and Polyoxazolines

Richard Hoogenboom

6.1

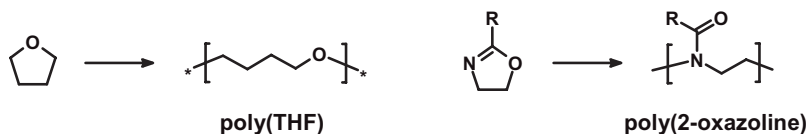
Introduction

Since the first report on ‘living’ polymerizations by Swarc in 1956 [1], much research effort has been focused on the synthesis and characterization of well-defined polymers. As a result, a large variety of ‘living’ and controlled polymerization techniques is available nowadays, including anionic polymerizations [2], controlled radical polymerizations [3–5] and cationic polymerizations [6, 7]. These ‘living’ and controlled polymerization techniques allow the synthesis of polymers with controlled length, monomer composition and monomer distribution, as well as different architectures such as star-shaped, comb and graft (co)polymers. The excellent control over polymer structures has resulted in the development of polymeric materials with novel properties based on, for example, the phase separation of incompatible blocks. An important class of ‘living’ polymerizations is the ‘living’ cationic ring-opening polymerization (CROP) of heterocyclic monomers, such as cyclic ethers and cyclic imino ethers. As a series of reviews has already (partially) covered the area of cationic ring-opening polymerizations (ROPs) of cyclic ethers and cyclic imino ethers [7–11], we will discuss in this chapter only the synthesis of polyethers and polyoxazolines, more specifically via the ‘living’ cationic ROP of the respective cyclic monomers. The major focus of this chapter will be on the polymerization mechanisms, as well as on recent progress of the ‘living’ CROP of the two most commonly studied monomers, namely tetrahydrofuran (THF) and 2-oxazolines (Scheme 6.1).

6.2

Polyethers

The synthesis of well-defined polyethers by ROP has only been reported for a limited number of monomers that have enough ring-strain to be readily opened, namely ethylene oxide, oxetane and THF. Moreover, the rather similar reactivity of the cyclic ether bonds and the ring-opened polymeric ether bonds in combination



Scheme 6.1 Cationic ring-opening polymerization of tetrahydrofuran (left) and 2-oxazolines (right).

with often highly reactive (cationic or anionic) propagating species facilitates the occurrence of transesterification reactions. As such, the development of ‘living’ ROP methods for cyclic ethers has been a challenging task. In this part, the ‘living’ polymerization of the three most commonly used cyclic ether monomers—ethylene oxide, oxetane and THF—will be discussed from a mechanistic point of view. In addition, different strategies for the preparation of functionalized poly(tetrahydrofuran) will be discussed.

6.2.1

Poly(ethylene Oxide)

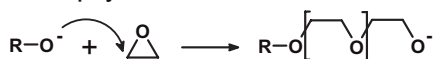
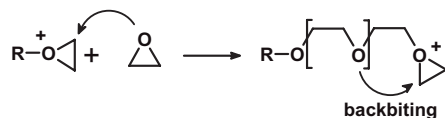
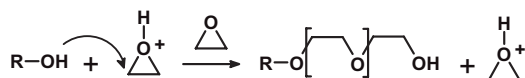
Poly(ethylene oxide) is the most commonly used polymer in personal, home and health care applications, due its water solubility in combination with a very low toxicity. These attractive properties of poly(ethylene oxide) can be ascribed to the distance between the alternating oxygen atoms in the chains that is in agreement with the hydrogen distances in liquid water allowing the formation of an extensive hydrogen-bonding network with water [12, 13].

The synthesis of well-defined poly(ethylene oxide) can be performed via a number of different ROP mechanisms, including both anionic [11, 14, 15] and cationic propagating species [11, 16]. For the preparation of well-defined polymer structures, the anionic mechanism is preferred as it proceeds without side reactions if stringent purification methods are applied for the reagents used. In contrast, the CROP of ethylene oxide should be performed via a cationic activated monomer approach instead of a chain-end activation approach, in order to reduce the back-biting processes that result in the formation of cyclic oligomers [11, 16, 17]. The occurrence of significant back-biting reactions is due to the relatively high nucleophilicity of the oxygen atoms in the polymer chain that could react with the cationic chain-end, rather than with the free monomer in solution. The use of an activated monomer approach can significantly reduce—but not completely eliminate—the occurrence of back-biting by reducing the amount of cationic chain-ends. As the anionic polymerization method is preferred for the preparation of well-defined (co)polymers, the cationic procedure is not often used nowadays. The different ROP mechanisms for the polymerization of ethylene oxide are depicted in Scheme 6.2.

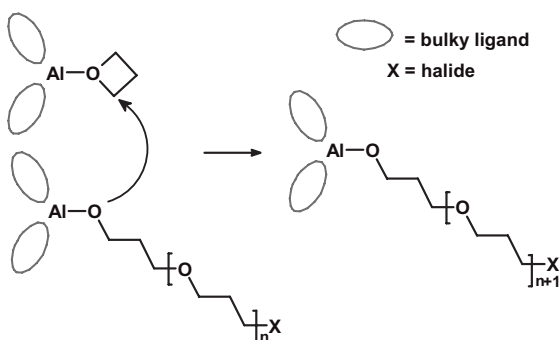
6.2.2

Poly(oxetane)

The most common application for the CROP of oxetanes is the crosslinking of coatings while only a very limited number of examples of well-defined

Anionic polymerization**Cationic chain-end polymerization****Cationic-activated monomer polymerization**

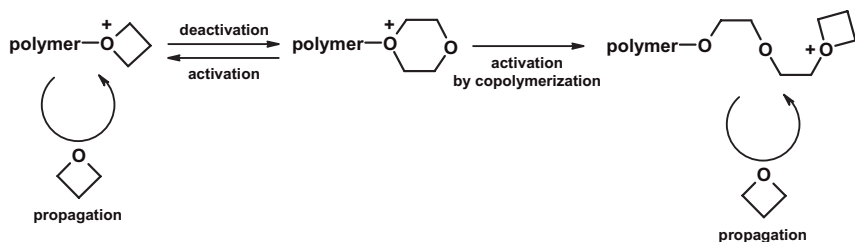
Scheme 6.2 Anionic, cationic chain-end and cationic activated-monomer ring-opening polymerization mechanisms for ethylene oxide.



Scheme 6.3 Living coordination anionic polymerization of oxetanes.

polyoxetanes have been reported. The first examples of the ‘living’ polymerization of oxetane were performed via a coordination anionic polymerization procedure using aluminum complexes with 5,10,15,20-tetraphenyl-21*H*,23*H*-porphine or organoaluminum diphenolates [18, 19]. The polymerization proceeds via aluminum alkoxides in combination with a monomer activation mechanism. The activated monomer will undergo anionic attack by the polymeric alkoxide groups, resulting in formation of the poly(oxetane) (Scheme 6.3). The bulky ligands around the aluminum center prevent the occurrence of intramolecular and intermolecular chain-transfer reactions by providing enough steric hindrance to obstruct the linear ethers from approaching the active center, while the cyclic species are not hindered.

More recently, another elegant approach was demonstrated for the ‘living’ CROP of oxetanes [20]. In order to prevent the occurrence of chain-transfer reactions, a nucleophilic solvent (1,4-dioxane) was used to end-cap the growing polymer chains, which resulted in chain-ends with lower reactivity. More specifically, the nucleophilicity of 1,4-dioxane is higher compared to the oxygen atoms in the polyether,



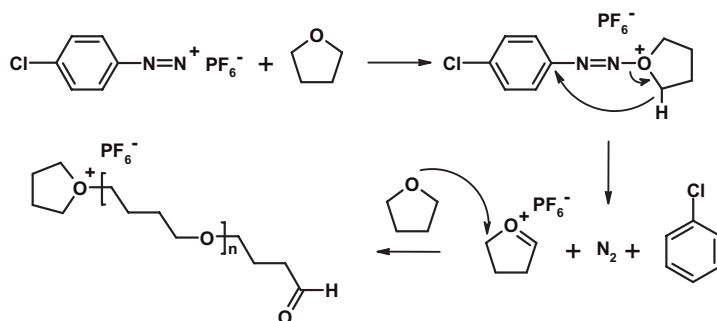
Scheme 6.4 Living cationic ring-opening polymerization of oxetane using 1,4-dioxane to control the nucleophilicity of the living chain-end to prevent the occurrence of chain-transfer reactions. Hexafluoroantimonate counterions are omitted for clarity.

but lower than the nucleophilicity of the oxetane. The proposed polymerization mechanism is depicted in Scheme 6.4. Although well-defined poly(oxetane)s could be prepared with up to $150\,000\text{ g mol}^{-1}$ and polydispersity indices below 1.3, a noticeable incorporation of the 1,4-dioxane into the polymers was observed above 50% monomer conversion, due to activation by copolymerization.

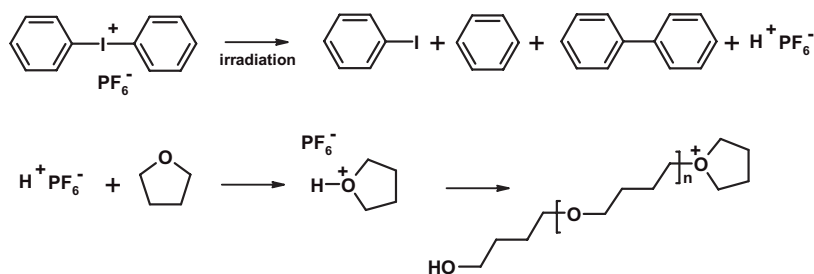
6.2.3

Poly(tetrahydrofuran)

The most-studied cyclic ether monomer in ‘living’ CROPs is THF. The slightly higher nucleophilicity of the monomer, when compared to the ring-opened polymer, facilitates a ‘living’ polymerization in the absence of chain-transfer processes when performed under the appropriate reaction conditions. A drawback of the rather similar nucleophilicity of the monomer and the polymer, however, is that the ceiling temperature for poly(tetrahydrofuran) is only 84°C ; that is, when the polymer is heated above 84°C depolymerization occurs, resulting in the monomer. An overview of the initial studies on the (‘living’) CROP of THF has been provided by Ledwith and Sherrington [21]. The livingness of the polymerization of THF was first demonstrated by Dreyfuss and Dreyfuss, using (*p*-chloro)benzenediazonium hexafluorophosphate as initiator [22, 23]. A linear increase in the logarithmic plot of intrinsic viscosity versus concentration of initiator was obtained which, in combination with the possibility of chain extension, demonstrated the ‘living’ character of the polymerization. In addition, mechanistic investigations revealed that initiation occurred via hydrogen abstraction of the THF by the chlorophenyl cation, as depicted in Scheme 6.5. The resulting oxonium ion further reacted with the monomer, which resulted in the ring-opened poly(tetrahydrofuran) bearing an aldehyde group at the beginning of the chain. Detailed kinetic investigations of the ‘living’ CROP of THF with this initiator were later performed at different temperatures [24], to reveal linear first-order kinetics, low polydispersity indices (below 1.10 when the polymerization was performed at -10°C), and an activation energy of 51.3 kJ mol^{-1} . More recently, a similar photo-induced polymerization method for the ‘living’ CROP of THF was reported using



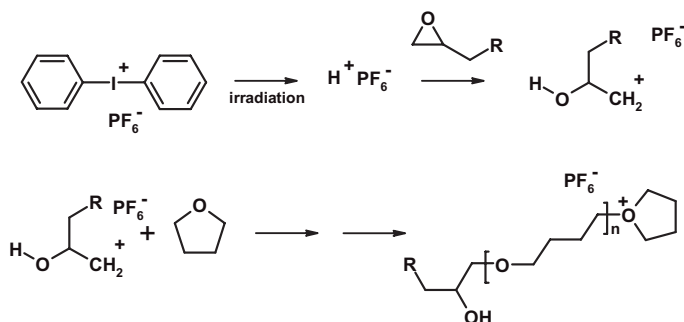
Scheme 6.5 Initiation mechanism for the *p*-chlorobenzenediazonium hexafluorophosphate-initiated living cationic ring-opening polymerization of tetrahydrofuran.



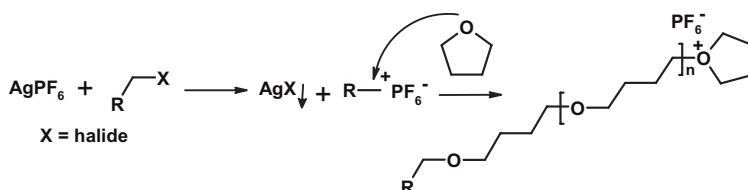
Scheme 6.6 Photoinduced cationic ring-opening polymerization of tetrahydrofuran using diphenyliodonium hexafluorophosphate as initiator.

dephenyliodonium hexafluorophosphate as initiator [25]. Upon photo-irradiation of this initiator, it releases a cationic proton that initiates the polymerization, as depicted in Scheme 6.6, yielding polymers with a hydroxy-functionality at the start of the chain. The advantage of the photo-induced polymerization method is that all chains will begin to grow at the same time upon irradiation and, thus, the time of initiation can be accurately controlled. The livingness of the photo-initiated polymerizations was demonstrated by a linear increase in molecular weight with conversion, as well as the possibility of chain-extending the polymer. Besides the direct initiating of poly(tetrahydrofuran), the addition of a functional ethylene oxide to the polymerization mixtures led to fast reaction of the released cationic proton to the ethylene oxide, followed by the ‘living’ polymerization of THF [26]. As a result, the functionality of the ethylene oxide was introduced at the start of the polymer chains, as depicted in Scheme 6.7. Similarly, the addition of a tetra-functional, star-shaped molecule bearing ethylene oxide units was used for the preparation of star-shaped poly(tetrahydrofuran).

The *in situ* formation of initiators for the cationic ROP of THF can be performed by the combination of organic halides with silver hexafluorophosphate salts, as depicted in Scheme 6.8 [27]. This procedure results in the formation of



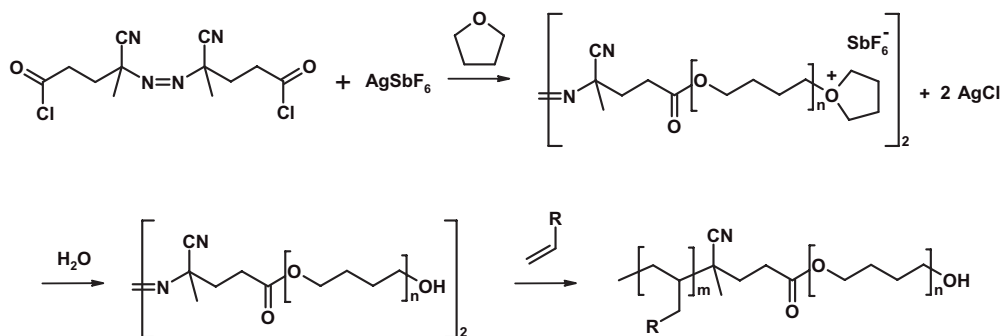
Scheme 6.7 Photoinduced cationic ring-opening polymerization of tetrahydrofuran in the presence of functional ethylene oxides, resulting in chain-end functionalized poly(tetrahydrofuran).



Scheme 6.8 Living cationic ring-opening polymerization of tetrahydrofuran initiated by the *in situ*-formed adducts of organic halides with Ag(I) hexafluorophosphate.

well-defined poly(tetrahydrofuran) using alkyl iodides, benzyl bromides and iodides, as well as allyl bromides and iodides. Organohalides with lower electrophilicity, such as aliphatic chlorides and bromides, resulted in slower exchange reactions and, thus, a slower initiation yielding polymers with relatively broad molecular weight distributions. The major advantage of the organohalide initiation method is the control over the polymer end-groups by varying the initiator, which was, for example, demonstrated by the use of bifunctional organohalide initiators [27]. A reactive bifunctional acid chloride initiator, having a diazo-linkage, was employed for the preparation of block copolymers by combination of 'living' CROP and (controlled) radical polymerization methods (Scheme 6.9) [28–30]. The 'living' CROP of THF was started by mixing THF solutions of 4,4'-azobis(4-cyanopentanoic acid chloride) precursor and Ag(I) hexafluoroantimonate. The resulting azide-containing polymer was subsequently applied as initiator for the (controlled) radical polymerization of styrene and methyl acrylate. The CROP of THF can also be performed with bromopropionyl bromide in the presence of Ag(I) triflate [31]. Upon termination of the polymerization with water, α -bromo- ω -hydroxy-poly(tetrahydrofuran) is obtained that can be subsequently used as macro-initiator for the atom transfer radical polymerization (ATRP) of styrene to yield poly(tetrahydrofuran)-*block*-poly(styrene) block copolymers.

In contrast to the previously described polymerization in bulk, Penczek and coworkers studied the CROP of THF in solution using various initiators and



Scheme 6.9 Synthesis of poly(tetrahydrofuran)-*block*-poly(vinyl monomer) via the combination of living cationic ring-opening polymerization and (controlled) radical polymerization techniques.

solvents [32–35]. The use of different solvent systems allowed the solvent polarity to be tuned, which greatly affected the proximity and stability of the ion pair at the ‘living’ chain end. The polymerization rate was found to increase with increasing solvent polarity due to a better solvation and stabilization of the ion pair by a polar medium. When using methyl triflate as initiator, an equilibrium between ionic and covalent propagating species is present (Figure 6.1), which is also influenced by the solvent polarity. In nitromethane, almost solely ionic propagating species are present, whereas in tetrachloromethane only 5% of the active centers are ionic species. Nonetheless, the polymerization almost exclusively occurs on the ionic species due its much higher reactivity compared to the covalent ester species. The equilibrium between cationic triflate species and covalent triflic ester species could be nicely demonstrated using ^1H NMR spectroscopy, as depicted in Figure 6.1. Besides the use of the commercially available methyl triflate, Goethals and coworkers demonstrated that functional triflate ester initiators could be prepared starting from the corresponding alcohols, triflic anhydride and 2,6-di-*tert*-butylpyridine as non-nucleophilic proton trap (Scheme 6.10) [36–38]. The use of less-electrophilic aliphatic triflates, compared to methyl triflate, resulted in a slow initiation of the THF polymerization and a nonlinear increase of molecular weight with conversion. When the electrophilicity of the initiator was enhanced by the use of allyl alcohol or benzyl alcohol precursors, a ‘living’ CROP of THF was obtained with linear first-order kinetics and a linear increase in molecular weight with conversion. The use of triflate initiators based on 1,4-bis(hydroxymethyl)benzene and 1,3,5-tris(hydroxymethyl)benzene resulted in the formation of well-defined, two-armed and three-armed poly(tetrahydrofuran), respectively [38].

Besides the use of different (functional) initiators for the ‘living’ CROP of THF, chain-end functionalities can be also introduced by terminating the polymerization by adding a nucleophile. When pyridine is added to the ‘living’ CROP of THF, the cationic propagating species will react with the pyridine base to form the pyridinium salt at the polymer chain-end (Scheme 6.11a) [39]. The scope of

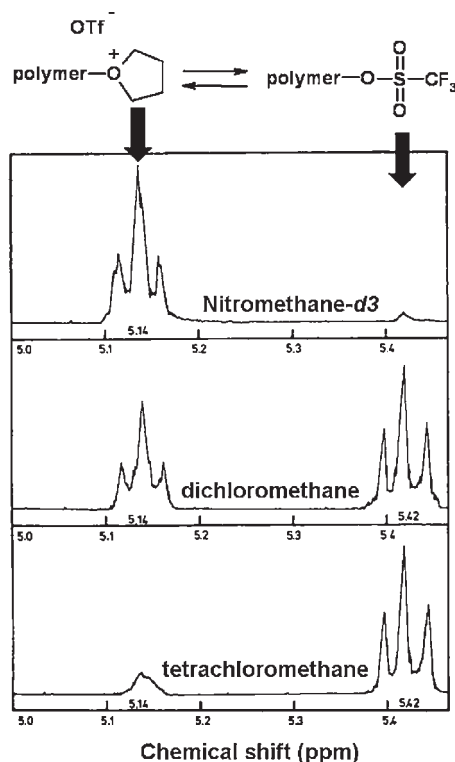
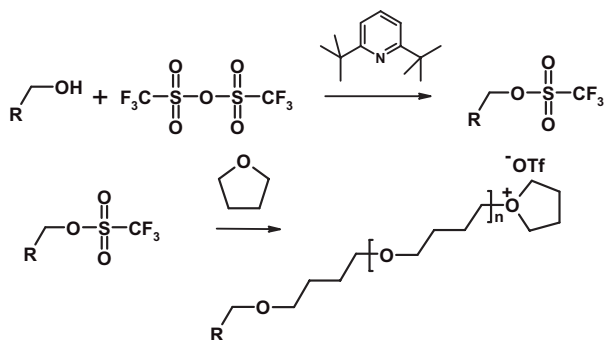
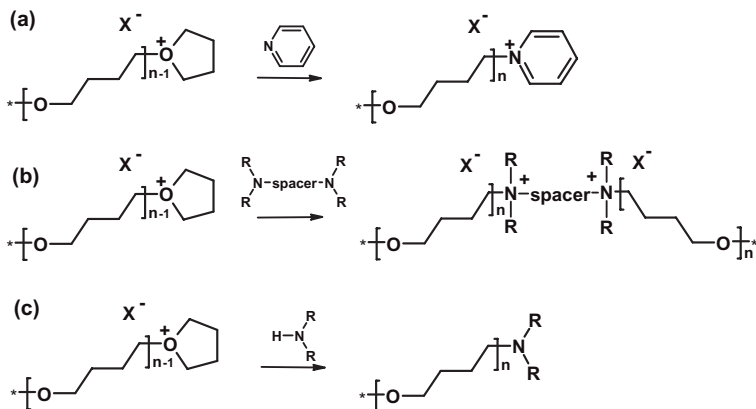


Figure 6.1 Top: Equilibrium between cationic and covalent propagating species for the living cationic ring-opening polymerization of tetrahydrofuran (THF) initiated with methyltriflate. Lower panels: ¹H NMR spectra obtained during the methyl triflate-initiated polymerization of THF in different solvents, demonstrating the different equilibria between cationic and covalent species. (Reprinted with permission from Ref. [33].)



Scheme 6.10 Synthesis of triflate-initiators from the corresponding alcohols by reaction with triflic anhydride in the presence of 2,6-di-*tert*-butyl pyridine as proton trap. OTf = triflate.

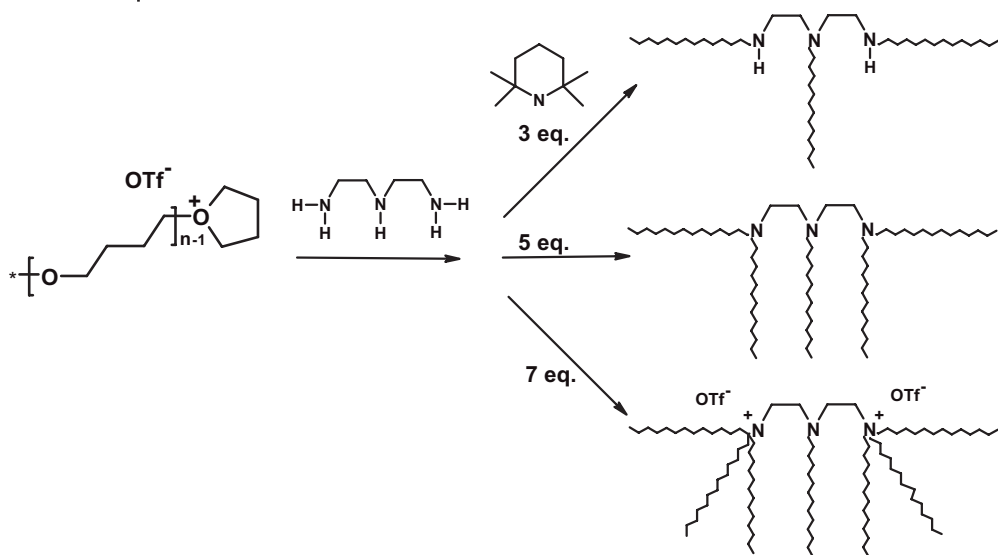
end-capping the 'living' poly(tetrahydrofuran) chains was further examined by using a range of tertiary [40], secondary [41] and primary [42] amines to terminate the polymerization of THF. A range of aromatic and aliphatic tertiary amines could successfully terminate the polymerization, resulting in ionic quaternary ammonium end-groups, whereby aromatic amines are less-reactive due to their lower



Scheme 6.11 End-capping of living poly(tetrahydrofuran) chains with various tertiary and secondary amines. (X^- represents the counterions).

basicity [40]. In addition, the use of bis-tertiary amine end-capping agents can be used for the formation of chain-extended poly(tetrahydrofuran) (Scheme 6.11b).

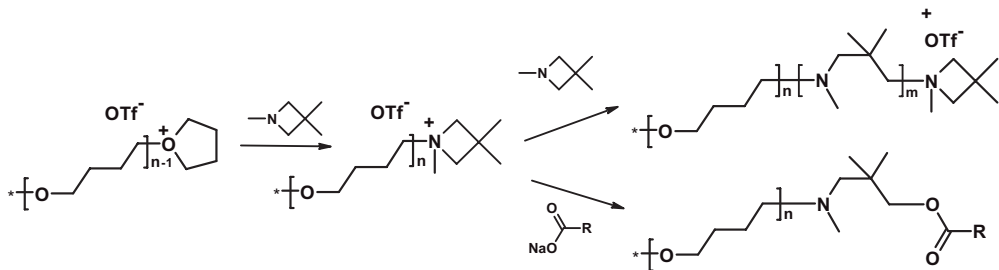
The end-capping of 'living' poly(tetrahydrofuran) chains with secondary amines can be used to prepare tertiary amine functionalized polymers (Scheme 6.11c). Similar to the use of tertiary amine terminating agents, the basicity of the secondary amines determines their reactivity in the end-capping reaction. Aromatic secondary amines, which exhibit very low reactivity, could be used for quantitative end-capping after activation with butyllithium. The tertiary amine end-group resulting from end-capping with secondary amines can be further utilized to end-cap 'living' poly(tetrahydrofuran), resulting in polymers with a charged quaternary ammonium group in the middle of the chains [41]. During the end-capping of 'living' poly(tetrahydrofuran) with primary amines, both the mono-adduct and bis-adduct can be formed, since the protonated secondary amine formed on the first 'living' polymer chain addition may equilibrate with free amines to yield the nonprotonated secondary amine. The latter can also act as a terminating agent for 'living' polymer chains, resulting in tertiary amines with two polymer chains [42]. In order to drive the end-capping reaction almost completely to the formation of mono-adduct, a 10-fold excess of the primary amine must be added. Nonetheless, the multiple addition of 'living' poly(tetrahydrofuran) chains to a single end-capper can be further exploited for the synthesis of star-shaped polymers [43, 44]. The 'living' CROP of THF was terminated by the addition of diethylene triamine as end-capping agent and 2,2,6,6-tetramethylpiperidine as proton trap [43]. The number of polymer chains that couple to the diethylene triamine could be varied from three to five and seven, depending on the amount of proton trap that was added into the mixture (Scheme 6.12). The solution and melt viscosity of the star-shaped polymers were shown to be significantly lower than for the linear analogues. The complexity of these systems could be further increased by using methacrylate- or allyl-functionalized triflate initiators to yield star-shaped polymers



Scheme 6.12 Synthesis of star-shaped poly(tetrahydrofuran) by end-capping with diethylene triamine in the presence of different amounts of 2,2,6,6-tetramethyl piperidine proton trap.

that were functionalized with double bonds on the periphery [45, 46]. These functional, star-shaped poly(tetrahydrofuran)s were then applied for the preparation of crosslinked polymer networks [45]. Star-shaped poly(tetrahydrofuran) was also prepared by terminating the 'living' polymerization with amine-functionalized dendrimers [44]. The number of polymer arms could be varied by changing the dendrimer generation or by changing the stoichiometry between the dendrimer and the number of 'living' chain ends. However, when the molecular weight of the 'living' polymer chains exceeded 2000 g mol^{-1} , only a limited number of chains could be grafted onto the dendritic cores due to steric hindrance. The possibility of terminating the polymerization of THF with amines was also applied to the preparation of block copolymers with aromatic polyamides [47, 48]. A mono-amine-functionalized aromatic polyamide, prepared by step-growth polymerization, was successfully used as the terminating agent for the 'living' polymerization of THF.

When the 'living' CROP of THF is terminated by the addition of strained cyclic tertiary amines, the reactivity of the chain ends is significantly lowered, which makes it insensitive to water, for example. Nonetheless, the low nucleophilicity of the resulting strained cyclic quaternary ammonium salts might be further explored for chain-end functionalization. Termination of the CROP of THF with azetidines was shown to yield, quantitatively, the corresponding quaternary ammonium salt functionalized poly(tetrahydrofuran) (Scheme 6.13) [49]. On adding more 1,3,3-trimethylazetidene (TMP) to the TMP-terminated polymer, the poly(tetrahydrofuran) was chain-extended with TMP, resulting in a well-defined block copolymer.



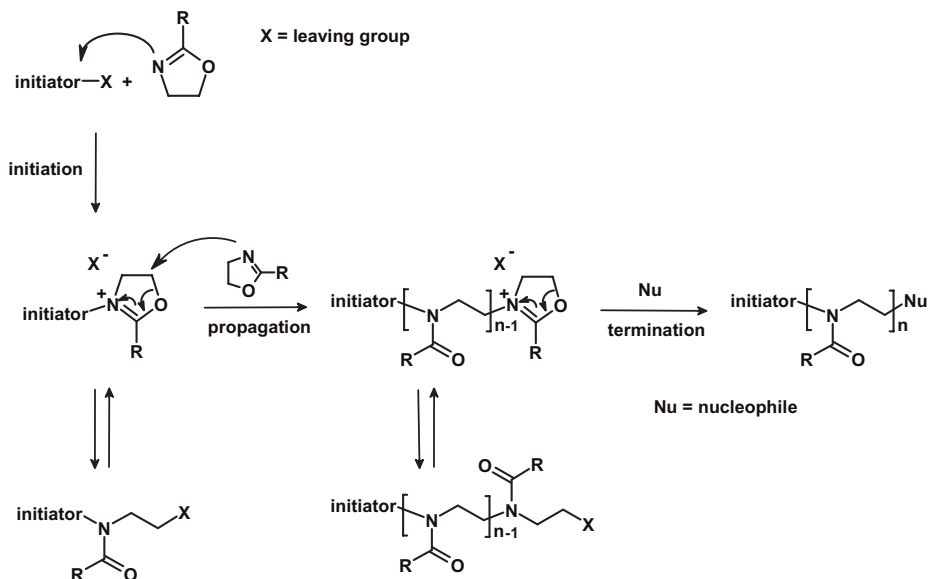
Scheme 6.13 End-functionalization of poly(tetrahydrofuran) with 1,3,3-trimethylazetidine and subsequent polymerization or functionalization.

Moreover, the TMP–poly(tetrahydrofuran) could be reacted with carboxylic acid sodium salts, and this resulted in a ring opening of the TMP moiety and attachment of the acid compound. Similar to the end-capping with TMP, terminating the living polymerization of THF with *N*-phenylpyrrolidine also resulted in stable nucleophilic cationic end-groups [50]. The subsequent reaction with carboxylic acid sodium salts was employed for the preparation of star-shaped polymers as well as poly(tetrahydrofuran) graft copolymers by reaction with poly(acrylic acid) sodium salt [51]. In contrast to the use of stable cationic intermediates, the ‘living’ cationic polymer chains can be also directly terminated by the addition of carboxylic acid sodium salts [31], dithiocarbamic acid sodium salts [52] or sodium alkoxides [53]. However, these direct functionalization approaches are more sensitive to traces of water or other impurities.

In recent years, the ‘living’ CROP of THF has mostly been performed using the commercially available methyl triflate or triflic anhydride [54] as initiator, in combination with water as terminating agent resulting in well-defined mono- or bis-hydroxyfunctionalized poly(tetrahydrofuran). However, these precursor polymers can be further used in a variety of different coupling reactions. The low glass transition temperature ($T_g = -86^\circ\text{C}$) of poly(tetrahydrofuran) makes it a suitable candidate for use as a soft block in thermoplastic elastomers [55–57]. The easy accessibility of such well-defined poly(tetrahydrofuran)s also led to their use in the preparation of supramolecular polymers, whereby the poor polymer properties of low-molecular-weight poly(tetrahydrofuran) could be significantly improved by combination with hydrogen bonding [58, 59] or metal–ligand interactions [60, 61].

6.3 Polyoxazolines

The CROP of 2-oxazolines was first reported in 1966 by four independent research groups [62–65]. The major advantage of the 2-oxazoline polymerization, compared to cationic cyclic ether polymerizations, is the large difference in nucleophilicity of the cyclic imine of the 2-oxazoline monomer and the amide of the ring-opened


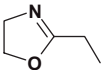

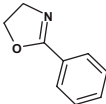



Scheme 6.14 Living cationic ring-opening polymerization of 2-oxazolines, indicating the equilibrium between covalent and cationic propagating species.

polymer. Hence, the polymerization can be performed over a wide range of temperatures, without the occurrence of significant chain-transfer reactions. In addition, the 2-substituent of the 2-oxazoline monomers can be easily varied, which strongly affects the polymer properties.

Under the appropriate conditions, the CROP of 2-oxazolines is known to proceed via a 'living' mechanism [8, 10]. In such an ideal 'living' polymerization, all polymer chains are initiated at the same time by nucleophilic attack of the free electron of the nitrogen atom in the 2-oxazoline monomer onto an electrophilic initiator, such as benzyl halide, methyl iodide, methyl tosylate and methyl triflate. Depending on the nucleophilicity of the monomer and the basicity of the initiator leaving group, a cationic or covalent propagating species is formed, as depicted in Scheme 6.14. Upon further monomer additions by nucleophilic attack to the propagating species, the ring-opened poly(2-oxazoline) is formed that still has the active propagating group at the chain end. On addition of a nucleophile, the polymerization can be terminated. Similar to the CROP of THF, functional groups can be introduced by using functional initiators or functional terminating agents. In addition, side-chain functionalities can be introduced by copolymerizing functional monomers. However, the relatively low nucleophilicity of the 2-oxazolines results in rather slow polymerizations at intermediate temperatures ranging from, for example, 16 h at 100 °C in *N,N*-dimethylacetamide [66] to several weeks in acetonitrile at room temperature [67]. Recently, it was shown that the use of higher temperatures (140–180 °C) in closed reactors, in combination with high monomer

Table 6.1 Types of propagating species in the cationic ring-opening polymerization of common 2-oxazoline monomers with different counterions. The nucleophilicity of the monomers decreases downwards; basicity of the counterions decreases to the right.

	Cl ⁻	Br ⁻	I ⁻	OTs ⁻	OTf ⁻
	Covalent [10]	Ionic [10, 71]	Ionic [10, 71]	Ionic [72, 73]	Ionic [10, 71]
	Covalent [74]	Covalent and ionic [74–76]	Covalent and ionic [74, 77]	Ionic [74, 78]	Ionic [10, 71]
	Covalent [10]	Covalent [10]	Covalent and ionic [79]	Ionic [79]	Ionic [10]
	– [71, 74]	Covalent [74]	Covalent and ionic [10, 74]	Ionic [74, 80]	Ionic [10, 71]
	–	–	Covalent [10]	Covalent [81, 82]	Ionic [81, 82]

loadings (~40 wt%), could accelerate the polymerization such that the reaction time was only a few minutes [68–70].

Although the equilibrium between covalent and cationic propagating species is strongly dependent on the polarity of the used solvent, the generally observed propagating species for a number of 2-oxazoline monomers are summarized in Table 6.1. The type of propagating species depends on the nucleophilicity of the monomer and the basicity of the leaving group of the initiator: When the basicity of the counterion is higher than the nucleophilicity of the monomer, covalent propagating species are present; however, when the basicity of the counterion is lower than the monomer nucleophilicity, cationic propagating species are formed. As a result, the most nucleophilic monomer, 2-methyl-2-oxazoline, forms cationic propagating species with all counterions except chloride [10, 71–73]. In contrast, the least nucleophilic 2-perfluoralkyl-2-oxazoline monomers cannot be polymerized with chloride or bromide initiators, and only cationic propagating species are formed with the least basic triflate counterions [10, 81, 82]. With certain initiators, the CROP of the monomers with intermediate nucleophilicity, namely 2-ethyl-2-oxazoline [71, 74–76], 2-unsubstituted-2-oxazoline [10, 79] and 2-phenyl-2-oxazoline [10, 71, 74, 80], demonstrated an equilibrium between the covalent and cationic

propagating species. However, the presence of covalent and propagating species is also heavily dependent on the solvent used. Although the polymerization of 2-methyl-2-oxazoline with bromide counterions commonly proceeds with cationic centers, it has been shown that the benzyl bromide-initiated polymerization of 2-methyl-2-oxazoline proceeds with 62% cationic species in nitrobenzene, and with less than 3% cationic species in tetrachloromethane. Nonetheless, even in the presence of such an equilibrium, propagation almost solely proceeds on the cationic species due its much higher electrophilicity compared to the covalent species [76, 83]. Pushing the solvent stabilization effect to its limits by the use of ionic liquids as extremely polar solvents results in an acceleration of the polymerization of 2-ethyl-2-oxazoline compared to its polymerization in acetonitrile, even though only cationic propagating species are present in both solvents [84].

Taking into account the large difference in reactivity of the family of 2-oxazoline monomers, the one-pot statistical copolymerization of selected monomer combinations results in the formation of quasi-diblock copolymers. This phenomenon was first demonstrated for the statistical copolymerization of 2-phenyl-2-oxazoline and the much slower 2-perfluoroalkyl-2-oxazoline [85, 86]. The 'living' cationic ring-opening copolymerization of these monomers (in nitromethane at 120 °C, initiated by methyl *p*-nitrobenzenesulfonate) resulted in a full conversion of the 2-phenyl-2-oxazoline after only 2 min, while almost no fluorinated monomer was incorporated. However, when the polymerization was continued for 40 h, the fluorinated monomer also reached full conversion and a relatively narrow monomodal molecular weight distribution was obtained, thus demonstrating the one-pot formation of a quasi-diblock copolymer. A faster alternative method was developed for the copolymerization of 2-phenyl-2-oxazoline and 2-perfluoroalkyl-2-oxazoline by a one-pot copolymerization with two-stage heating. The first polymerization stage, which was performed at 60 °C, resulted in the polymerization of 2-phenyl-2-oxazoline, after the full conversion of which the temperature was increased to 150 °C; this resulted in a polymerization of the 2-perfluoroalkyl-2-oxazoline monomer. The initiator and monomer conversion during this two-stage heating polymerization clearly demonstrated the formation of a quasi-diblock copolymer (Figure 6.2). Similarly, the one-pot statistical copolymerizations of 2-phenyl-2-oxazoline with the more nucleophilic 2-methyl-2-oxazoline or 2-ethyl-2-oxazoline at 140 °C yielded quasi-diblock copolymers in which first the 2-methyl-2-oxazoline or 2-ethyl-2-oxazoline was incorporated, followed by incorporation of the slower 2-phenyl-2-oxazoline [87]. However, the smaller difference in nucleophilicity for these monomer combinations resulted in a broader transition regime in which the two monomers were mixed in comparison to the copolymerization of 2-phenyl-2-oxazoline with the fluorinated monomer.

The 'living' nature of the CROP of 2-oxazolines allows the preparation of well-defined block copolymers by the sequential monomer addition method; that is, after full conversion of the first monomer, a second monomer can be introduced resulting in the formation of diblock copolymers (Scheme 6.15) [88, 89]. When this procedure is repeated several times, triblock [90, 91] and tetrablock copolymers [92] are readily accessible. By using a similar sequential procedure, diblock and triblock copolymers consisting of both poly(tetrahydrofuran) and poly(2-oxazoline)

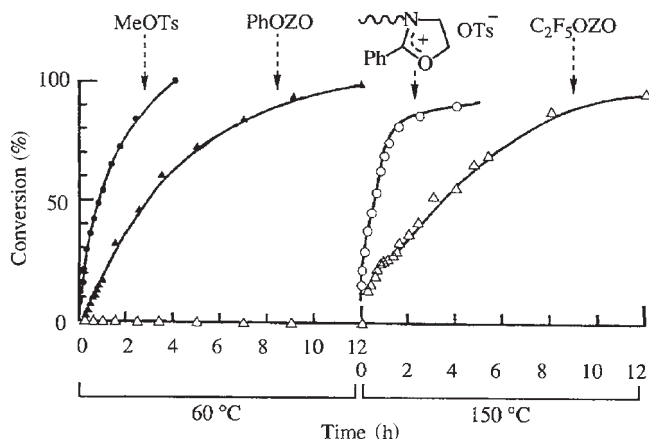
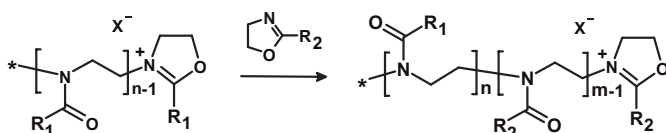


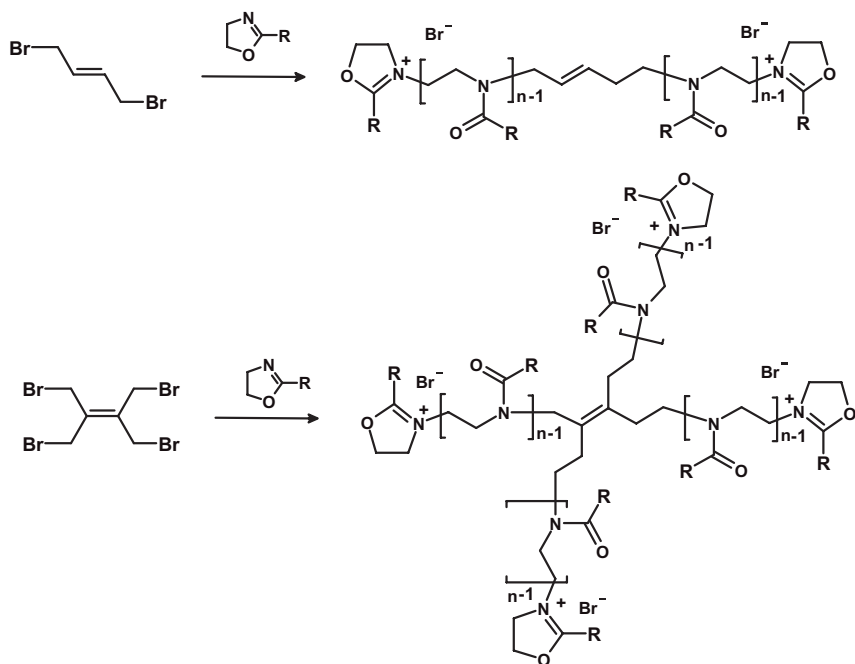
Figure 6.2 Time-conversion curves of the initiating species and the monomers in the one-pot, two-stage heating copolymerization of 2-phenyl-2-oxazoline and 2-perfluoroalkyl-2-oxazoline. (Reprinted with permission from Ref. [86].)



Scheme 6.15 Synthesis of poly(2-oxazoline) block copolymers by the sequential monomer addition method.

segments can also be prepared, whereby the polymerization of THF with the more reactive onium salt should be performed first to ensure complete initiating of the 2-oxazoline block [93, 94].

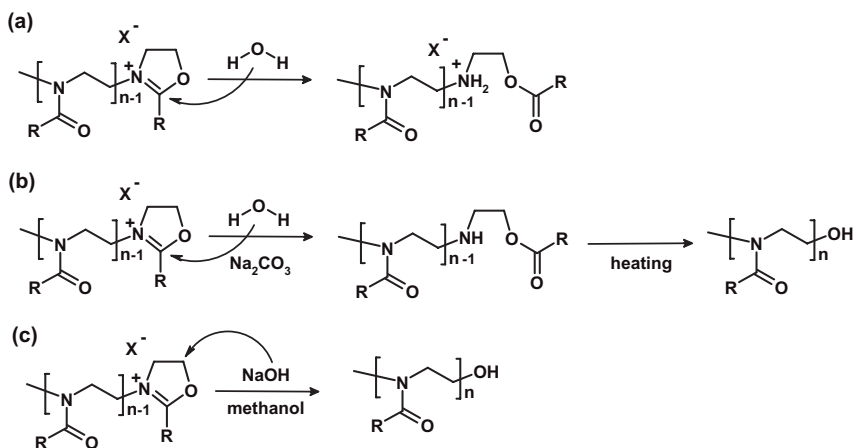
The use of functional initiators is a common method for the synthesis of chain-end functionalized poly(2-oxazoline)s. Allyl-functionalized poly(2-oxazoline) can be prepared by initiating the polymerization with allyl-tosylate, which can be further converted into trimethoxy-silane by a hydrosilylation reaction [95]. Alternatively, poly(2-oxazoline) macromonomers can be prepared by the use of vinyl ester [96] or styrenic [97] initiators. These macromonomers can be used as comonomers in free radical copolymerizations resulting in polymers with grafted poly(2-oxazoline) chains [97, 98]. α -Amino- ω -hydroxy-poly(2-oxazoline)s can be prepared by initiating the polymerization with a phthalimido-functional tosylate initiator and termination with sodium hydroxide, followed by conversion of the phthalimido-group into an amine by treatment with hydrazine [99]. Besides these functional groups that can be used for further coupling reactions, poly(2-oxazoline)s bearing sugar [100], fatty acid [101], perfluoroalkyl [102], anthracene [103] and silesquioxane [104] terminal groups have also been prepared by using functional initiators. Similarly, the use of multifunctional initiators can be applied for the synthesis of star-shaped poly(2-oxazoline)s. The use of dibromoallyl was successfully applied as a bifunctional initiator, while tetrabromoallyl yielded four-armed, star-shaped polymers (Scheme



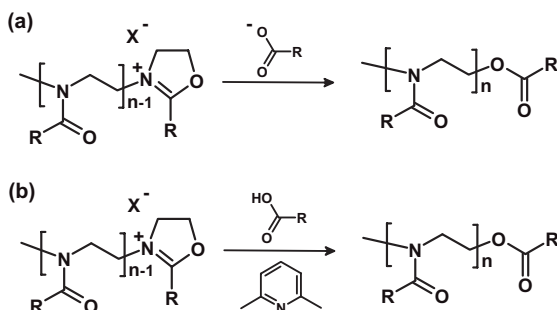
Scheme 6.16 Multi-armed poly(2-oxazoline)s using multi-bromo allylic initiators.

6.16) [105]. Multifunctional initiators based on, for example, cyclotriphosphazine [106], silsesquioxane [107], porphyrin [108] and bipyridine metal complex [109, 110] cores were also successfully used for the 'living' cationic ring-opening (co)polymerization of 2-oxazolines, resulting in star-shaped (co)polymers. The use of polymeric initiators also allowed the construction of well-defined complex macromolecular architectures, such as triblock copolymers with a non-poly(2-oxazoline) middle block that is used to initiate the 2-oxazoline polymerization after functionalization with tosylate end-groups [111–113]. In addition, poly(2-oxazoline) graft copolymers can be prepared by the initiation of the CROP from, for example, poly(chloromethylstyrene) [114, 115] or tosylated cellulose [116].

Next to the use of functional initiators, the presence of an electrophilic propagating species in the 'living' CROP of 2-oxazolines also allows functionalization of the poly(2-oxazoline) by the addition of a nucleophilic terminating agent (see Scheme 6.14). Surprisingly, the addition of water as nucleophile does not directly yield hydroxy-functionalized polymers; rather, the water attacks the 2-position of the cationic propagating species, resulting in the formation of an ester end-group (Scheme 6.17a) [78, 117]. Upon termination with sodium hydrogen carbonate the same hydrolysis product is obtained, which can be further isomerized to the hydroxy-functionalized polymer (Scheme 6.17b) [118]. The ester amine is formed as kinetic product, which could be explained by a stereoelectronic theory of the intermediate structures while the amide alcohol is the thermodynamic product

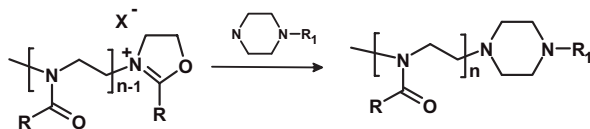


Scheme 6.17 Termination of the living poly(2-oxazoline) chains by the addition of water (a), Na_2CO_3 in water followed by isomerization to the hydroxyl-functionalized polymer (b) and sodium hydroxide in methanol (c).



Scheme 6.18 End-capping the living poly(2-oxazoline) chains by the addition of carboxylic acid salts (a) or by the *in situ* formation of the carboxylic acid salts from the acid and 2,6-dimethylpyridine (b).

[119]. Alternatively, quenching the living CROP with an aqueous or methanolic sodium hydroxide solution directly yields the hydroxyl-functionalized polymers (Scheme 6.17c) [10, 67]. Obviously, such hydroxy-terminated polymers are ideal starting materials for further functionalization [10, 67, 118]. Termination of the ‘living’ polymerization of 2-oxazolines can also be performed by the addition of carboxylic acid salts (Scheme 6.18) [118]. Besides using a preformed carboxylic acid salt, the salt can also be prepared *in situ* by the addition of both the carboxylic acid as well as 2,6-dimethylpyridine that acts as a proton scavenger [120]. The sterically hindered 2,6-dimethylpyridine did not terminate the ‘living’ polymer change, whereas attempts to use pyridine as a proton scavenger yielded polymers that were terminated with the pyridinium salt. The final class of nucleophiles that are often



Scheme 6.19 Synthesis of chain-end-functionalized polymers by terminating the living poly(2-oxazoline) chains with piperazine derivatives.

applied as terminating agents for the ‘living’ CROP of 2-oxazolines are amines. On addition of a primary amine to the polymerization mixture, a secondary amine is formed upon reaction of the amine with the cationic oxazolinium chain end [118]. This approach has been used to couple amine-functionalized styrene moieties to poly(2-oxazoline)s, resulting in macromonomers [121]. In addition, quenching the ‘living’ polymerization with an excess of ethylenediamine yields primary-amine functionalized polymers [122]. Such an amine-functionalized poly(2-methyl-2-oxazoline) has been used as precursor for the preparation of poly(2-methyl-2-oxazoline)-*block*-poly(amido-amine) dendrimer. Furthermore, terminating the polymerization of 2-methyl-2-oxazoline with amine-functionalized cellulose yields poly(2-oxazoline) grafted cellulose [123]. Nonetheless, terminating the polymerization with primary amines yields functionalized polymers that still contain a secondary amine that might also react with an additional polymer chain and, therefore, the use of secondary amines might be preferable. The use of piperidine as terminating agent for the living polymer chains was found to result in fast (<10 min) and quantitative termination [124]. Based on this first report, a number of functionalized piperazines have been employed to introduce functional chain-ends to poly(2-oxazoline)s (Scheme 6.19), including styrene [125, 126], amines [127] as well as terpyridine metal-coordinating ligands [128]. When tertiary amines are employed as the terminating agents, cationically charged end-groups are introduced into the polymer chains [120, 124]. The introduction of cationically charged quaternary ammonium end-groups to poly(2-methyl-2-oxazoline)s can be used for the formation of polymers with antimicrobial properties [129, 130].

Another major advantage of poly(2-oxazoline)s is that, next to the easy access to well-defined (block co)polymers and chain-end functionalized polymers, the polymer properties can be significantly altered by changing the substituent on the 2-position of the 2-oxazoline ring. The large effect of the side chain on the polymer properties can be easily illustrated by the water-solubility of the poly(2-methyl-2-oxazoline), poly(2-ethyl-2-oxazoline), poly(2-isopropyl-2-oxazoline) and poly(2-*n*-propyl-2-oxazoline), whereas larger substituents result in hydrophobic polymers. In addition, poly(2-methyl-2-oxazoline) and poly(2-ethyl-2-oxazoline) are biocompatible and show ‘stealth’ properties in the body, similar to poly(ethylene oxide) [131, 132]. Moreover, the poly(2-ethyl-2-oxazoline), poly(2-isopropyl-2-oxazoline) and poly(2-*n*-propyl-2-oxazoline) each exhibit a lower critical solution temperature [67, 133, 134]. The thermal as well as the surface properties of the poly(2-oxazoline)s are also heavily dependent on the substituents of the 2-oxazoline monomer [78]. More complex 2-oxazoline monomers with, for example, oligo(ethylene oxide)

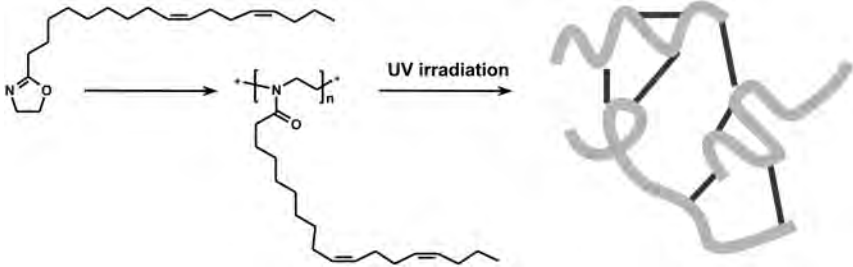
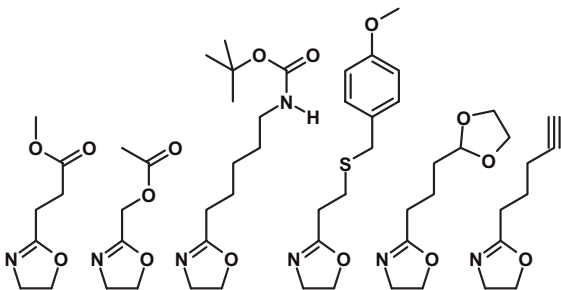
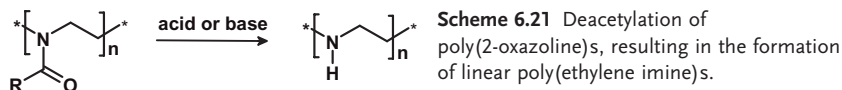


Figure 6.3 Polymerization of 2-unsaturated fatty acid-2-oxazoline and the subsequent oxidative crosslinking of the unsaturated sites by UV irradiation.



Scheme 6.20 Overview of some of the (protected) functional 2-oxazoline monomers that have been used successfully in the living cationic ring-opening polymerization.

[135], saturated [135] or unsaturated [136] fatty acid-based substituents, can also be used in the ‘living’ CROP. Such unsaturated fatty acid side chains are not affected by the CROP, and thus the resulting polymers can be crosslinked (Figure 6.3) [137]. The crosslinking of such fatty acid-based materials can be performed by UV-curing, which results in the formation of mainly ether and peroxy crosslinks and also (to a smaller extent) C–C crosslinks via an oxidative free radical mechanism [138–140]. A similar strategy was also applied for the preparation of core crosslinked micelles based on poly(2-ethyl-2-oxazoline)-*block*-poly(2-unsaturated fatty acid-2-oxazoline) [141]. A number of 2-oxazoline monomers with (protected) functional groups in the side chains have also been reported (Scheme 6.20). Copolymerization of these monomers with other nonfunctional monomers results in polymers having a predefined number of side-chain functional groups that can be used for further coupling reactions. For most of the functional groups, such as acids, alcohols and amines, a protected monomer must be used in the polymerization due to their nucleophilicity. The synthesis and polymerization of 2-oxazoline monomers with protected acid and alcohol functionalities was originally reported back in 1968 [142] but, more recently, aldehyde [143], amine [144], alkyne [145] and thiol [146] -functionalized 2-oxazoline monomers have also been synthesized and successfully utilized in the ‘living’ CROP.



Besides the synthetic aspects of the preparation of (functional) poly(2-oxazoline)s, it is noteworthy to mention that poly(2-oxazoline)s are well-known precursors for the preparation of linear poly(ethylene imine)s upon hydrolysis under either alkaline [147] or acidic [148] conditions (Scheme 6.21). Detailed kinetic investigations on the acidic deacetylation of poly(2-oxazoline)s have revealed that both partial and full deacetylation can be achieved by varying the stoichiometry between the acid and the cleavable groups [149]. Furthermore, partial cleavage of the side chains can be controlled by selective acidic hydrolysis based on the easier hydrolysis of poly(2-ethyl-2-oxazoline) compared to poly(2-[4-*tert*-butylphenyl]-2-oxazoline) [150].

6.4

Summary and Prospects

As described in this chapter, the ‘living’ CROP of THF and 2-oxazolines are versatile methods for the preparation of well-defined polymers, whereby both the initiation and termination steps provide the possibility of introducing a variety of functional groups. Poly(tetrahydrofuran) has a low T_g , and is often used as soft block in for example, thermoplastic elastomers. As such, it is expected that the ‘living’ CROP of poly(tetrahydrofuran) will remain an important method in the preparation of soft polymeric materials, whereby the easy introduction of functional groups can be used to prepare novel functional materials.

In contrast to poly(tetrahydrofuran), the properties of poly(2-oxazoline)s can be easily tuned by varying the substituent in the 2-position providing access to, for example, hydrophilic and hydrophobic polymers as well as polymers with low and high T_g -values. This versatility of poly(2-oxazoline)s—as well as the easy access to (multi)block copoly(2-oxazoline)s—should lead to a renewed interest in this class of polymer during the coming years, perhaps resulting in novel functional materials that are based on the thermoresponsive behavior of certain poly(2-oxazoline)s. In addition, the biocompatibility and stealth properties of poly(2-methyl-2-oxazoline) and poly(2-ethyl-2-oxazoline) make them suitable candidates to replace poly(ethylene glycol) in the preparation of drug–polymer conjugates, as well as protein-repellant coatings.

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7

Polyamides*Jan Roda***7.1****Introduction**

Polyamides (PAs, except for those that are fully aromatic) represent a versatile group of plastics that have been successful for 70 years in the market of fibers, engineering plastics and specialties. Aliphatic polyamides and copolyamides (Scheme 7.1), obtained by a classical polycondensation of diamines and diacids, or α -amino acids (PA 66, PA 612, PA 610, PA 46, PA 11) or by the hydrolytic polymerization of lactams (PA 6, PA 12), belong to the group of highly valued semicrystalline plastics that are widely used in most branches of industry; in some applications they are, as yet, irreplaceable.

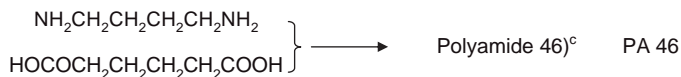
The preparation of PA 66 has been known since 1937 [1], while that of PA 6—by the polymerization of ϵ -caprolactam (CL)—was first described in 1938 [2]. The primary information regarding the anionic polymerization of CL (which forms the basis of this chapter), appeared in 1941 [3].

In 2005, the total global production of aliphatic polyamides reached 7.1 Mt, of which 4.1 Mt was accounted for by PA 6, 2.7 Mt by PA 66, and 300 kt by specialized (high-performance) polyamides [4]. The distribution of consumption for PA 6 and PA 66 is shown in Table 7.1 [4].

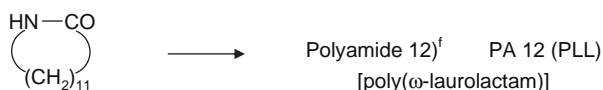
According to the data for its annual production, PA 6 lies between specialty and commodity plastics, although its physico-mechanical and chemical properties are superior to many commodity plastics. Currently, some two-thirds of all PA 6 and PA 66 production is processed to fibers, with the remainder being used as a valuable construction material (engineering plastics).

The corresponding polymerizations have, therefore, been the subject of many excellent reviews, books, encyclopedias and monographs [5–11]. At present, these activities are focused on improving the step polymerization (polycondensation) that yields PA 66, together with its modifications. The hydrolytic polymerization of CL has also been studied in detail, and current research in this area is predominantly applications-oriented. From both theoretical and practical standpoints, the anionic polymerization of lactams continues to show great promise, due to its

Step growth process



Chain growth process



Scheme 7.1 An overview of basic aliphatic polyamides.

^aPoly(iminoadipoyl-iminohexamethylene);^bPoly(iminohexamethylene-iminosebacoyl); ^cPoly(iminoadipoyl-iminotetramethylene); ^dPoly[imino(1-oxoundecamethylene)];^ePoly[imino(1-oxohexamethylene)];^fPoly[imino(1-oxododecamethylene)].

Table 7.1 Consumption of PA 6 and PA 66 and related application fields.

	PA 6 (Mt)	PA 66 (Mt)
Fiber	2.6	1.6
Resin	1.2	1.1
Film	0.31	0.04

sensitivity with regards to initiation, polymerization procedure and temperature. Hence, the door remains wide open in terms of both basic and applied research into PAs, with much remaining still to be discovered.

The anionic polymerization of CL offers a unique possibility to perform a procedure below the polymer's melting point ($\sim 215^\circ\text{C}$), thus enabling the creation of a product with a low content of low-molar-mass portions [6]. On the other hand,

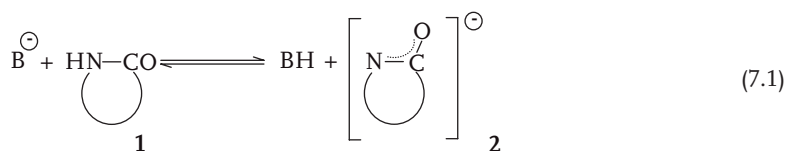
this is one of the rare cases where an anionic polymerization proceeds in the monomer melt at temperatures well above 100 °C.

Whilst this chapter is based largely on the anionic polymerization of lactams (CL), using information gathered from a range of excellent—and often unsurpassable—reviews [7–9], it also incorporates the details of some interesting findings made over the past two decades.

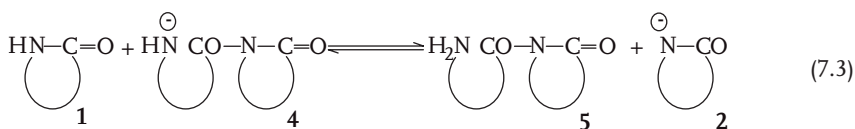
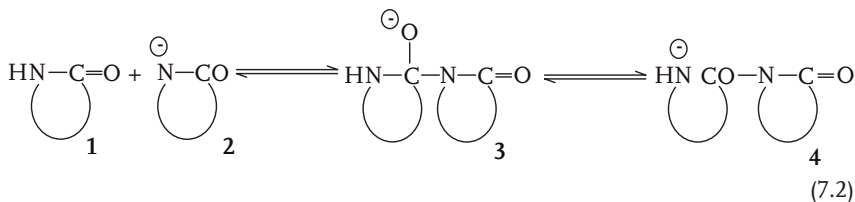
7.2

Mechanism of the Anionic Polymerization of Lactams

The mechanism of the anionic polymerization of lactams has been studied mainly for CL—the most easily accessible (and industrially produced) lactam. The basis for the mechanism of anionic polymerization of lactams is fixed [5, 12–14], and differs from ‘conventional’ anionic polymerization. The process involves addition of the monomeric lactam anion (the so-called ‘anionically activated monomer’) onto a nonionic growth center located at the end of the growing chain. Thus, lactam anion 2 is formed by the reaction of a proper nucleophile with lactam 1 (Equation 7.1):



Through a slow reaction between lactam 1 and its anion 2, followed by a rapid neutralization of the aminic anion 4, ω -aminoacyllactam 5 is formed and the lactam anion is recovered (Equations 7.2 and 7.3)



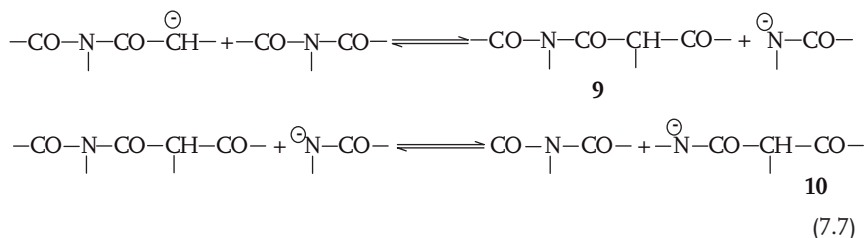
The propagation then proceeds as a repeated nucleophilic attack of the anionically activated monomer onto the activated endocyclic carbonyl group of the (non-ionic) growth center (acylation of the lactam anion) (Equations 7.4 and 7.5).



The growth centers of the *N*-acyllactam structure can be alternatively introduced into the system or formed by a proper reaction *in situ*, which causes a manifold increase in the rate of propagation. The polymerization initiated by a combination of the lactam anion and *N*-acylated lactam is referred to as ‘activated’ (assisted).

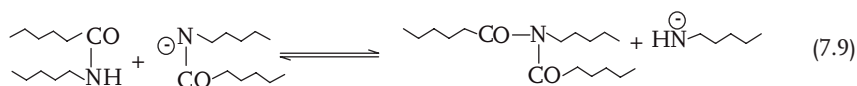
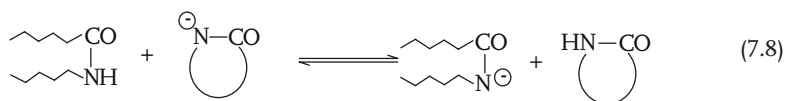
The acidic character of the α -hydrogen atoms (with respect to the carbonyl groups of *N*-acyllactam growth center) is comparable to the acidity of hydrogen of the $-\text{CONH}$ group; after an equilibrium between the C and N anions has been established (Equation 7.6), side condensation reactions of the Claisen type occur [7–9], which can be represented in a simplified manner, as in Equation 7.7.





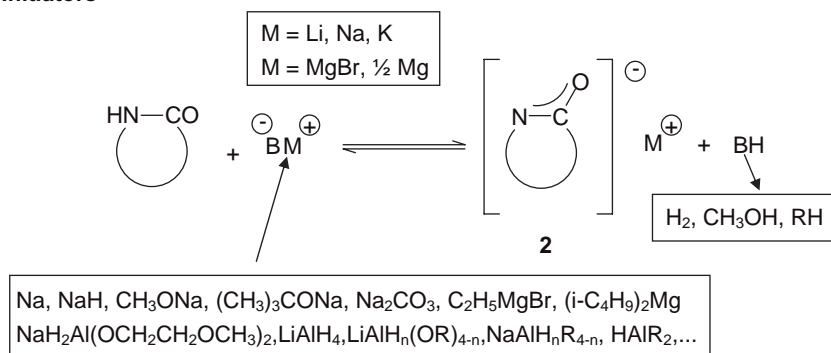
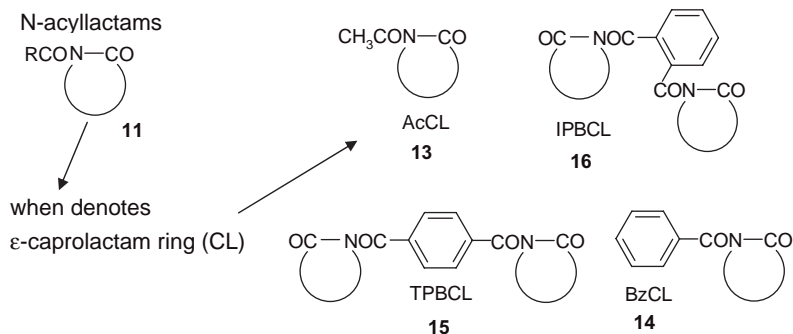
N-acylated derivatives of 2-oxoamides (ketoimides) **9**, and subsequently 2-oxoamides (ketoamides) **10**, are formed; these are the key derivatives and lower the concentration of the components of the initiation system. Here, each condensation step consumes two molecules of classical growth centers during the formation of one ketoimide structure. As its acidity is distinctly higher than that of the amidic group, this leads also to a decrease in the concentration of lactam anions, and hence in the concentration of the initiator. The ketoamides at higher temperatures decompose to yield isocyanates, to form uracil structures and water (the latter being an inhibitor of the polymerization process), and so on [9, 12].

In addition, equilibrium is established between amidic anions of lactam and those of the polymer chain, which leads to further (reversible) acylation reactions, branching of the polymer and formation of the amino end-groups (Equations 7.8 and 7.9).



The result of this complex system of reversible and irreversible side reactions is the simultaneous consumption and partial recovery of both components of the initiation system, a reduction in its activity, the formation of irregular (thermally or hydrolytically instable) structures in polymer chains, and last—but not least—the creation of branched structures. Such branching leads, in the case of multifunctional activators, to partial gelation.

The formation of the ketoimide/ketoamide side structures (**9** and **10**) in polymer chains can be deduced from model experiments with low-molecular-weight materials, as well as from the isolation of several types of aminoketone formed from polymeric ketoamide structures following total hydrolysis of the polymer, for example $\text{NH}_2(\text{CH}_2)_5\text{CO}(\text{CH}_2)_5\text{NH}_2$ [9]. An easier method to monitor (qualitatively) these side products is to measure the UV spectra of the polymer solutions over the 270–280 nm range, using absolute formic acid (HCOOH) as a solvent. By

Initiators**Activators:** monofunctional, difunctional, polyfunctional**Precursors****Substances****Scheme 7.2** Components of the initiation system for the activated anionic polymerization of lactams.

comparing the absorbances, the differences in side-structure content in the materials can be estimated [6, 17].

From what has been described above (and summarized in Scheme 7.2), the fact that the anionic polymerization of lactams actually proceeds and indeed yields quality products may seem to be a ‘small miracle’!

The anionic polymerization of lactam (e.g. CL) can be performed in two different temperature modes. Polymerization in the melt of the lactam below the melting point of polymer is characterized by polymerization, followed by crystallization. However, sometimes—depending on the initial polymerization temperature—the formation of polymer is accompanied simultaneously by crystallization. In both

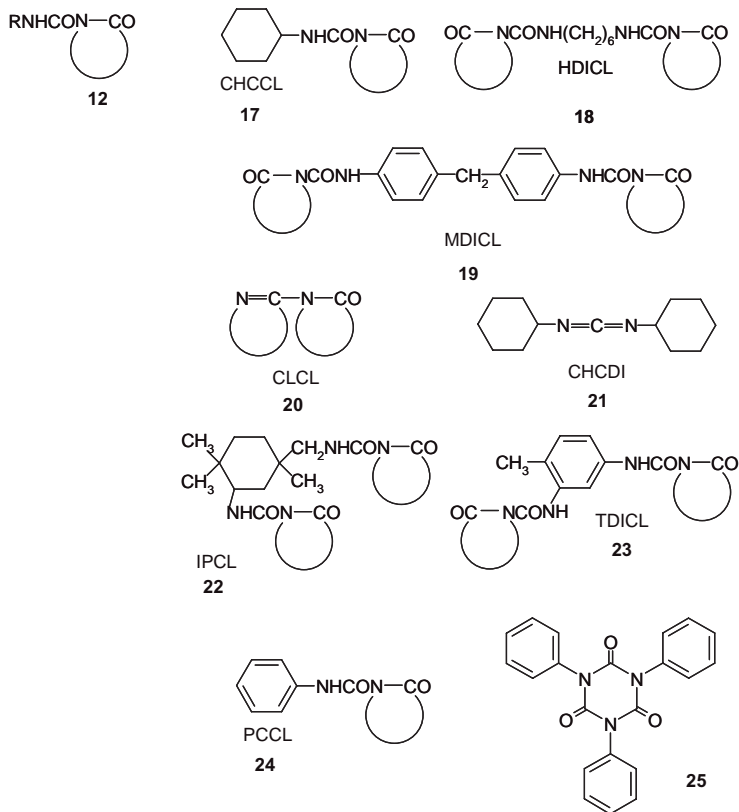
N-carbamoyllactams

Figure 7.2 Continued

cases, solidification of the polymerization feed takes place at relative low monomer conversions such that the equilibrium content of unreacted monomer and oligomers is set up, but is actually regulated only by the amorphous phase of the PA. In the case of CL, for a temperature interval of 140–190 °C the content of low-molecular-weight fractions will fluctuate by 2–4 wt%.

Above the melting temperature of the polymer (PA 6 = 215 °C; PA 12 = 180 °C) the equilibrium is established in a one-phase system. In the melt and for CL polymerization the equilibrium content of the monomer and water-extractable oligomers reaches 8–10 wt% (see Section 7.6). On the other hand, the content of extractables for poly(ω -laurolactam) is only 2 wt% and it is not necessary to remove this from the crude product.

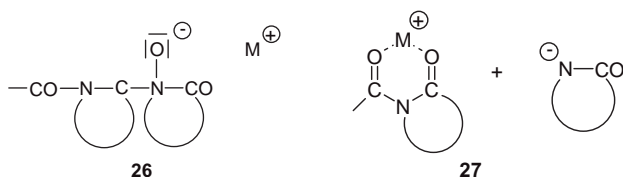
Another advantage in selecting a polymerization temperature below the melting temperature of the polymer is that virgin polymers, when prepared, contain higher proportions of crystalline phase (40–50%) than do those polymers that are crystallized from the melt (30–40%).

7.3

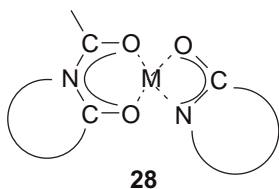
Initiators for the Anionic Polymerization of Lactams

Anionically activated monomer (in the form of a salt of lactam; see Scheme 7.2, Initiators) can be isolated in a pure form (*extra situ* procedure), although in most cases it is prepared *in situ*, using suitable nucleophiles [8] (see Scheme 7.2). In order to prepare the sodium salt of ϵ -caprolactam, it is possible to apply metallic Na, NaH, CH_3ONa , NaOH and sodium *tert*-butoxide. For the synthesis of the salts of lactams through the reaction with alkoxides or hydroxides, it is necessary to shift the equilibrium by removing alcohol or water (by distillation), which may affect the quality of the initiator, especially when the solution is overheated. During recent years, the sodium salt of CL, concentrated to the corresponding lactam, has been available on an industrial basis ($\sim 1.3 \text{ mol kg}^{-1}$).

Due to the complexity of the dissociation equilibria, several mechanisms leading to an incorporation of the lactam anion into the polymer chain have been suggested [8, 12]. In most cases, the concept of the tetrahedral intermediate **26** is preferred, originating by an attack of the lactam anion onto the endocyclic carbonyl group of the growth center:



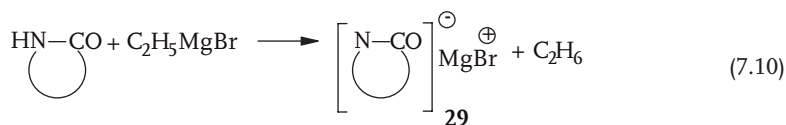
For the lactamolytic mechanism [14], a complexation of the cation with the growth center is assumed **27**, whereas the ion-coordinative mechanism [15] includes a formation of a complex between the growth center and the lactamate **28**:



The individual mechanism depends heavily on the type of lactam, initiator and activator, on the temperature of the reaction, on the permittivity of the reaction medium, and the higher temperatures being favorable for the effect of free ions [18, 19].

ϵ -Caprolactam magnesium bromide (CLMgBr) **29**, in combination with *N*-acyllactam activators, forms 'successful', fast-acting initiation systems for the reaction injection molding (RIM) technology (in the case of CL, this is referred to as the Nyrin process) [20]. The process is characterized by a balanced participation

of propagation, exchange and side reactions in a polymerization mixture consisting of CLMgBr **29**, isophthaloyl-bis- ϵ -caprolactam (IPBCL) **16** and α,ω -dihydroxyterminated copolyethers. This is also the reason why, at the present time, CLMgBr is commercially available, again in the form of a concentrate in solid monomer (~ 1 mol kg $^{-1}$). For the laboratory-scale process it can be successfully substituted with ethylmagnesium bromide:



The properties of CLMgBr **29** have been explained by lower nucleophilicity of the salt, and also by the extent of dissociation and formation of ion pairs, in fact by the coordination caused by MgBr^+ as counterion. It is likely that these effects, together with a lower participation of side reactions, cause the PA 6 prepared by a fast adiabatic process with *N*-acetyl- ϵ -caprolactam (AcCL **13**) to yield a polymer, the M_w of which was only twice that predicted by theory [21]. The activation energy of the polymerization was 30 kJ mol^{-1} [22], as compared to the usual value of $60\text{--}80 \text{ kJ mol}^{-1}$, found for ‘classical’ initiation systems using alkaline salts [8].

By using AcCL **13** and CLMgBr **29**, which was synthesized *in situ* by the reaction of lactam with $\text{C}_2\text{H}_5\text{MgBr}$, PA 6 chains having an unusual M_w in the range of $7\text{--}9 \times 10^5 \text{ g mol}^{-1}$ were prepared (at 150°C) [23].

The initiation activity of systems such as CLNa/HDICL **2/18** and CLMgBr/AcCL **29/13** are both comparable and very fast at 150°C , with the system CLMgBr/HDICL **29/18** showing a long induction period that can be explained by the slow conversion of *N*-carbamoyl centers into the *N*-acyllactam counterparts [24]. The induction period of the CLMgBr/HDICL **29/18** system determines the period of processability of the polymerization feed.

In an elegant study [25], the role of side reactions was explored, their relatively low occurrence being as expected for CLMgBr at 150°C . The comparison of CLNa **2** and CLMgBr **29** (activator *N*-benzoyl- ϵ -caprolactam **14**) reflects a totally different situation; with identical conversion, the degrees of polymerization are comparable and substantially higher than theory; hence, in both cases a part of the growth centers must be consumed in the side reactions. This is in perfect agreement with the determined content of aminoketones, formed from Claisen-like side structures by a total hydrolysis of PA 6 (Table 7.2), and which provides a measure of the consumed *N*-acyllactam structures.

Both systems have similar extent of side reactions; in other words, they are not decreased substantially by CLMgBr [20]. However, the result of a polymerization in the presence of 20% α,ω -dibenzamidopoly(propylene oxide) (the model of Nyrim block-copolymer preparations; see the last two lines in Table 7.2) was surprising with, in the case of CLMgBr, the polyether present unexpectedly suppressing the side reactions. Thus, the data provided by others [25] represent a classical

Table 7.2 Comparison of side reaction extent for different initiators.

	γ_w	$P_{n,m}$	$P_{n,t}$	$[AK]_m$	$[AK]_t$
CLNa	96.6	261	138	3.45	3.67
CLMgBr	97.7	226	140	2.68	2.56
CLNa ^a	79.0	201	113	0.99	0.31
CLMgBr ^a	94.5	204	134	0.09	0.24

γ_w , degree of conversion after 30 min, 150 °C.

$P_{n,m}$, determined by viscometry.

$P_{n,t}$, calculated $P_{n,t} = \gamma_w/[A]_0$, A-activator.

$[AK]_m$, real content of side structures.

$[AK]_t$, theoretical content of aminoketones.

$[AK]_t = [A]_0 - \gamma_w/P_{n,m}$.

^a 20 wt% poly(propyleneoxide) added.

demonstration of the sensitivity of the process conditions to anionic polymerization, though some principles and phenomena cannot be anticipated.

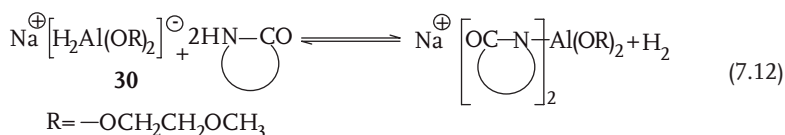
The high activity of CLMgBr **29** can be explained as a consequence of the coordination of initiator to the growth centers (intermediate **28**) [26], due to the coordination the electrophilicity and the reactivity of the growth center (the rate of addition of lactam anion to the nonionic growth centers) is increased. It is also necessary to take into account the so-called Schlenk equilibrium, which effect cannot be neglected:



On the other hand, although the polymerization activity of CL_2Mg is very low, MgBr_2 can coordinate with the growth center and thus increase its reactivity. Formation of the complex MgBr_2 with CL or η -capryllactam [27–29], MgBr_2 /linear aliphatic amide, MgBr_2 /N-butyryl- ϵ -caprolactam [28] has unequivocally been proven. The effect of coordination must be substantial and driving because the CL_2Mg alone is a very slow initiator [30]. Another interesting characteristic of Mg initiators is the marked suppression of cyclic oligomer formation [31].

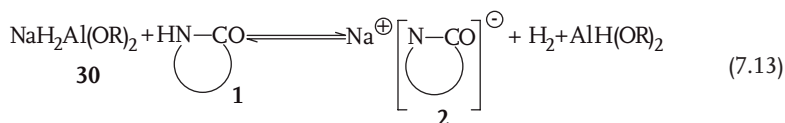
Another extensively studied group of compounds that yield anionically activated monomer includes complex hydrides (see Scheme 7.2) and also $\text{NaAlH}_2(\text{OCH}_2\text{CH}_2\text{OCH}_3)_2$ —this is sodium bis(2-methoxyethoxy)aluminum hydride **30**, the so-called ‘Synhydride’.

Whilst the main advantage of Synhydride [32, 33] is its liquid state (it contains 20–25% toluene), a drawback is the evolution of hydrogen during preparation of the initiator. However, this was overcome by using a preparation which was the product of the reaction between 1 mol of Synhydride and 2 mol of CL, which proved to be much safer from a technological standpoint (Equation 7.12), so-called ‘Dilactamate’:

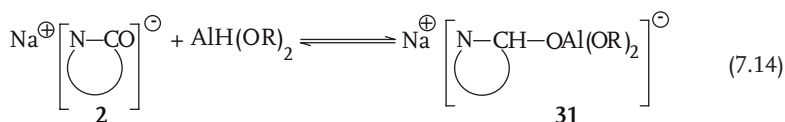


It was proved some time later [34] that if 1 mol Synhydride was reacted with 2 mol of CL, then, on completion of the reaction, 1 mol of unchanged CL could be detected in the mixture. The structure suggested in Equation 7.12 is, therefore, controversial.

An attempt to explain the mechanism of action of Synhydride has been made [34] wherein it was assumed that Synhydride first formed a classical lactam salt and $\text{AlH}(\text{OR})_2$ (Equation 7.13):

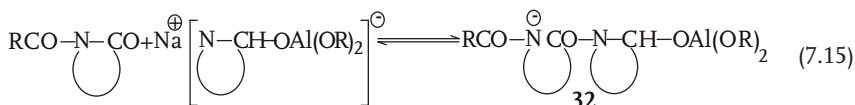


All of the evidence collected showed that only the lactam ion could react with the $\text{AlH}(\text{OR})_2$ formed, such that a reduction occurred (Equation 7.14):

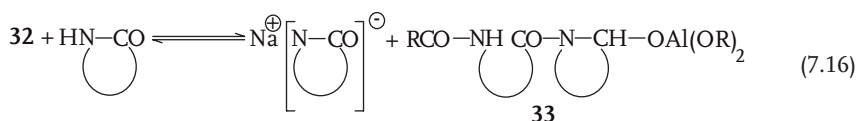


The sodium salt of 2-(dialkoxy aluminioxy)-1-(azacycloheptanone) **31** may thus be responsible for the lower nucleophilicity of the initiator.

When only **31** is present in the system then, by reacting with the activator, it should yield **32** (Equation 7.15):



This step was proved convincingly by monitoring with infrared (IR) spectroscopy. In similar fashion to the classical mechanism, **32** is neutralized by the reaction with lactam to **33**. The reaction is in equilibrium, such that the concentration of the lactam anion is given by the content of the polymer (Equation 7.16):



According to the mechanism proposed, the lactam anion reacts immediately with the $-\text{OAl(OR)}_2$ end group, whereupon **31** is regenerated and added again onto the *N*-acyllactam end-group. In this way, each propagation group is preceded by a reduction of the lactam anion. This step of the mechanism, although supported by several experiments, appears—to say the least—‘unusual’, and is surely open to discussion.

The data obtained for the Synhydride/4,4'-diisocyanatodiphenylmethane (MDI) **19**-initiated polymerization of ω -lauro lactam were processed mathematically according to the mechanism proposed and, when the Claisen condensation reactions were included, a perfect agreement with the experimental data was found [35].

The lower nucleophilicity of the initiator derived from Synhydride was successfully utilized for the synthesis of block copolymers, such as PA 6-*b*-poly(dimethyl siloxane) [36].

Although Synhydride (resp. Dilactamate) is not considered to be a ‘normal’ initiator, it is today being used in industrial polymerization casting to some extent (private confidential communication). Recently, Synhydride has been applied, in combination with diisocyanate activators, for the preparation of powder polyamides (see Section 7.10).

7.4

Activators for Anionic Polymerization of Lactams

The main function of an activator is to increase the rate of polymerization through supplying nonionic growth centers. Substances bearing the *N*-acyllactam structure are denoted as ‘direct’ activators, while compounds forming the nonionic growth centers only in the polymerization feed are referred to as ‘indirect’ activators, being the precursors of the growth centers. The basic types, together with some examples, are summarized in Scheme 7.2.

Although, at the first sight, only the first propagation step depends on the structure of the activator, while the next steps proceed repeatedly on the same *N*-acyllactam group, the total rate of polymerization depends notably on the chemical structure of the activators. This invokes the magic and complexity of the anionic lactam polymerization—the activators introduce various end-groups into the polymer chains, influence the permittivity of the polymerization medium, are subject to side reactions (which change their instantaneous concentrations basically in the initial stage of polymerization), affect the dissociation of the initiator, and so on [7–10]. Consequently, the behavior of the initiation

systems of anionic polymerizations—and above all of CL—cannot be fully predicted.

7.4.1

***N*-Acyllactams**

N-Acyllactams (NAL) **11** represent a group of activators of CL polymerization that have been studied in depth, mostly in combination with alkali salts of lactams, and CLMgBr. The most relevant reports have focused on the kinetics, the degree of polymerization of the polyamide (P), the yield (conversion), transformation of the growth centers and the participation of side reactions, both in isothermal and adiabatic regimes and in the temperature range of 100 to 240 °C [7–10].

Isothermal studies (140–160 °C) of the polymerization of CL (below the melting temperature of PA 6) initiated by CLNa and by both aliphatic and aromatic *N*-acyllactams [37], showed an apparent zero-order kinetic with respect to monomer, at least up to 60% conversion; the apparent rate constant increased in the order *N,N'*-terephthaloyl-bis- ϵ -caprolactam (TPBCL; **15**) < *N*-benzoyl- ϵ -caprolactam (BzCL; **14**) < *N*-acetyl- ϵ -caprolactam (AcCL; **13**) < *N*-hexanoyl- ϵ -caprolactam < *N*-butyryl- ϵ -caprolactam. The dependences of P on conversion were linear up to high conversions, and weakly temperature-dependent, which suggests that the process has a ‘pseudo-living’ character. However, the reduced numbers of polymer molecules differ substantially for individual activators, which in some cases confirms the distinct drop in growth center concentration through side reactions. For example, in the case of *N*-acetyl- ϵ -caprolactam **13** and *N,N'*-terephthaloyl-bis- ϵ -caprolactam **15**, the decrease is 60% and 90%, respectively. The number of polymer molecules (NPM), from which the change in the number of growing or formed polymer chains can easily be deduced, is defined as $NPM = 10\gamma_w/113P_n(\text{mmol g}^{-1})$, where γ_w is the conversion (in %), P_n is the number-average degree of polymerization, and 113 corresponds to the molar mass of CL; here, the fraction $NPM/[A]_0$ is the reduced number of polymer molecules mentioned above, where $[A]_0$ is the initial activator concentration, and reflects the change of the number of the initial growth centers during polymerization. The decrement of centers takes place predominantly at the beginning of the process, most likely in the homogeneous stage. The typical activation energy of polymerization is about 70 kJ mol^{−1}.

At polymerization temperatures above the melting temperature of polymer, the polymerization reaches the equilibrium content (~90%) of polymer within a few minutes; however, prolonged heating of the polymerization mixture causes degradation, which is seen as a rapid decrease in the molar masses.

7.4.2

***N*-Carbamoyllactams**

N-carbamoyllactams (NCL) **12**—the most frequently used activators—include isolated (individualized) NCL and their precursors (substances containing the

isocyanato group). In most cases, industrially available mono- and diisocyanates serve as a source for pure NCL (see Scheme 7.2).

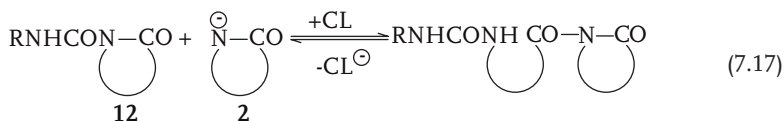
In general, NCL belong to the most effective and rapidly acting activators. Aliphatic isocyanates or aliphatic NCL operate more quickly than their aromatic counterparts (for the alkali salts of CL as initiators) although, at the same time, NCL are more active than NAL [38, 39].

These rapid systems are used predominantly for (adiabatic) polymerizations below the melting point of PA 6. These cases allow one to prepare PA6 (97% conversion) with more than 40% crystallinity, often with both α and γ phases. If difunctional NCL are used, for example, 1,6-di(carbamoyl- ϵ -caprolactam)hexane, HDICL 18, the polymer product contains up to 80% of gel (insoluble in $\text{CF}_3\text{CH}_2\text{OH}$), which improves the mechanical properties [16, 17, 40].

Probably the most rapid isocyanate, cyclohexylisocyanate (17), affords PA 6, which is basically free of side structures (according to UV analysis); the formation of the polymer is kinetically controlled [16].

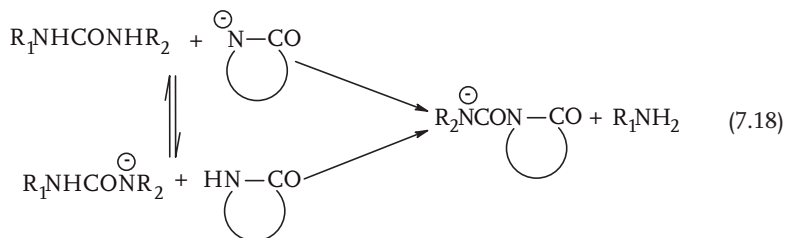
The fact that NCL are more active than NAL can be explained also by the acidity of the *N*-carbamoyl groups, the difference of NCL and CL in $\text{p}K_a$ being seven orders of magnitude [41].

Formally, the propagations for NCL and NAL differ in the first step only, after which the end-groups appear to have the structure of *N,N'*-disubstituted urea (Equation 7.17).



Although the $\text{p}K_a$ values of *N,N'*-dialkyl derivatives of urea are comparable with that of CL, the (semi)aromatic derivatives of urea are substantially more acidic [41, 42]. Model polymerizations performed at 150–170°C and initiated by CLNa 2 and AcCL 13 are accelerated by *N,N'*-diphenyl-, *N,N'*-dibutyl- and *N*-phenyl-*N'*-butylurea more than would be expected from their independent activation effects [43]. This could be ascribed not only to the ‘controlling’ of the system basicity, but also to a formation of new growth centers. The change in permittivity of the reaction medium may also enhance the dissociation of the salt, although a modification (complexation) of the growth center cannot be excluded, either.

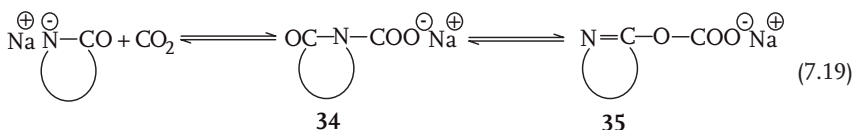
The only urea derivatives mentioned above can also act as activators of CL polymerization although, when compared to NAL 11, the rate of the process is lower by an order of magnitude [43]. The initial apparent rate constant of the propagation increases with increasing relative acidities of the urea derivatives; in spite of this, values of P_n are similar for all cases. The growth centers are formed by the acylation of the corresponding anions and an equilibrium between the lactam and urea anions must be established (Equation 7.18).



7.4.3

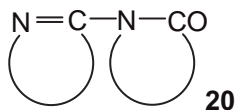
Special Activators

Since the 1960s, carbon dioxide has belonged among the activators; in a gaseous state, it is introduced into the polymerization feed containing an initiator, so that a part of the salt is transformed to the carboxylate growth centers. As yet, it has not been decided if N- or O-carboxylate **34**, **35** is formed [44] (Equation 7.19).



Carboxylates have found wide application in the anionic polymerization of 2-pyrrolidone [45] (see Section 7.12). With CL, CO₂ was used especially for the preparation of powder-like PA 6 (Section 7.10).

The O-structure of the carboxylate seems to be supported by other 'exotic' but successful activators containing an iminolactam (acylamidine) structure.



According to kinetic analyses, these activators, in combination with alkali salts of CL, dose the growth centers at a constant rate [46] and do not transform to the growth centers immediately, as in the case of NCL **11** or NAL **12**.

The growth centers from carbodiimides are formed through the reaction with an alkali salt, and have the guanidine structure (Equation 7.20). These systems are a part of liquid single-component initiation systems of anionic polymerization of lactams [47].



Carbamates should also be mentioned here as indirect activators; they act more slowly (by an order of magnitude) than NCL do are comparable with NAL, with an

7



S



r

619

r

t

the product very quickly assumes a statistical structure (Section 7.9). Elegant evidence for the formation of growth centers, as well as for the participation of transacylation reactions, is represented by the successful polymerization of CL initiated by poly(ϵ -caprolactone) with CLMgBr as an initiator [40].

Non-homopolymerizing γ -butyrolactone (BLO) behaves at 150 °C in a totally different way; it is a slow activator, and is not incorporated into the PA 6 chains. Rather, higher concentrations of BLO retard the polymerization [38].

7.5

Nonactivated Polymerization

During the nonactivated polymerization, the nonionic growth centers are formed continuously through a slow reaction between the lactam and its anion (see Equation 7.2), and their concentration is at least one order of magnitude lower than the initial concentration of the salt. The process is therefore characterized by a distinct induction period and a markedly lower rate than the activated polymerization. The key component here is the initiator, which has a crucial effect on the course of the polymerization process. On the other hand, it is an excellent kinetic tool for assessing the quality of the initiation, the purity of the system and the monomer, and the suitability of the experimental technique applied, and so on.

From a comparison of the course of the nonactivated polymerization of CL, it can be concluded that the initiator prepared *in situ* through the reaction of CL and a methanolic solution of CH_3ONa [41] is somewhat less active than the carefully isolated sodium salt of CL [42]. The apparent activation energy ($E_a = 230 \text{ kJ mol}^{-1}$) was determined for the initial, self-accelerating stage of the polymerization [41]. The second stage, characterized by formal zero-order kinetics with respect to monomer, shows an activation energy of 120 kJ mol^{-1} , which is close to the E_a of the activated polymerization. For both stages of the polymerization, the orders of the reactions with respect to initiator concentration are nonintegral and temperature-dependent, which indicates the existence of an unusually complex reaction mechanism. This is reflected also in the dependence of P_v on the degree of conversion that passes through a maximum at approximately 80% polymer conversion.

The absence of a self-acceleration period [43] is a common feature of nonactivated anionic polymerizations initiated by magnesium-containing compounds (CL_2Mg , CLMgBr or $\text{C}_2\text{H}_5\text{MgBr}$). The activity of CLMgBr is markedly higher than that of CL_2Mg , and depends significantly on the mode of preparation [44]. In contrast to the initiation by CLNa [41], when the maximum attainable conversion corresponds to the equilibrium at a given temperature, in the case of an initiation by CL_2Mg , CLMgBr or $\text{C}_2\text{H}_5\text{MgBr}$, a limiting content of polymer is established, which is distinctly lower than would correspond to the relevant equilibrium. The suppression of the formation of cyclic oligomers is also a very interesting feature of these polymerizations [24].

The nonactivated polymerizations differ also in the extent of the inhibitory effect of water. In a CLNa-initiated polymerization, the polymerization system is able to reach the content of polymer at the equilibrium, if the water content

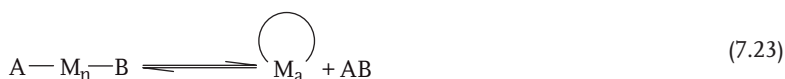
does not exceed the half-value of the initial concentration of the initiator, but the self-acceleration period of polymerization extends and P_n markedly decreases [45]. The nonactivated anionic polymerization of CL, as initiated by the magnesium-based compounds, is substantially less sensitive towards water. In contrast, with an increasing concentration of water the limiting content of the polymer falls markedly.

7.6

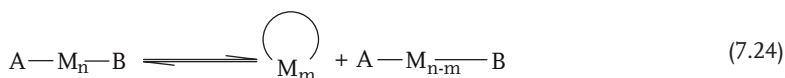
Cyclic Oligomers of ϵ -Caprolactam

Generally, irrespective of the reaction mechanism, the polymerizations of lactams direct towards a state of an equilibrium between linear (macro)molecules, monomer, cyclic oligomers and initiator. The equilibrium products of CL polymerization contain, depending on the polymerization temperature (180–280°C), between 0.8 and 3.5 wt% of cyclic oligomers [6, 46, 47], in addition to 2–8 wt% of the unreacted monomer. If the total content of these low-molar-mass components exceeds 2–3 wt%, they must be removed from the polymer because they may have an unfavorable influence on both the processing and application properties of PA.

The chemical structure of the initiator used determines the type of the active centers of the polymerization, which not only serve as the centers for the growth of polymer chains but also participate in cyclization reactions. The extent of reactivity of the active centers is directly responsible for the content and distribution of macrocycles during the course of the polymerization. The most important reactions leading to cyclic oligomers are mutual reactions of the end-groups of linear molecules ('end-biting') (Equation 7.23)



and intramolecular reactions of the end groups with amidic groups inside the chain ('back-biting') (Equation 7.24).



The effect of initiator type on the formation of cyclic oligomers manifests itself very markedly in the nonactivated anionic polymerization of CL [24]. When the process is initiated by the sodium salt of lactam, the formation of macrocycles is kinetically controlled; the concentration of the cycles pronouncedly exceeds the equilibrium values, in similar fashion to cationic polymerization. In contrast, when the magnesium salts of CL or ethyl magnesium bromide are used as initiators, a considerable suppression of cyclization reactions was demonstrated for

polymerizations, both below and above the melting temperature of the polymer formed. (During polymerization, the dimer concentration was an order of magnitude lower than in a comparable stage of polymerization initiated by the sodium salt of lactam.) A weaker tendency to form cycles can probably be explained by the coordination of Mg-based compounds with the end-groups of linear polyamide molecules [24]. This assumption is indirectly confirmed by the existence of coordination compounds of magnesium bromide with CL, amides and NALs (Section 7.3).

The cyclic dimer and the trimer of CL are able to change the crystalline structure in the solid phase, depending on temperature. On the basis of the results of a structural study of two identified forms of a CL cyclic dimer [48] and three forms of a CL cyclic trimer [49], a relationship between temperature-dependent changes of their conformational structure and changes of supramolecular structure was described.

In an anhydrous medium at 260 °C, the cyclic trimer undergoes transamidation reactions leading to a polymer, cyclic oligomers and monomer, even faster than does CL [50]. Under the same conditions, the transamidation reactions of the dimer are complicated by its extremely high melting temperature (345 °C). The low reactivity of the cyclic dimer represents the main problem encountered when processing the mixture of oligomers, which represents the waste material from the production of hydrolytic PA 6.

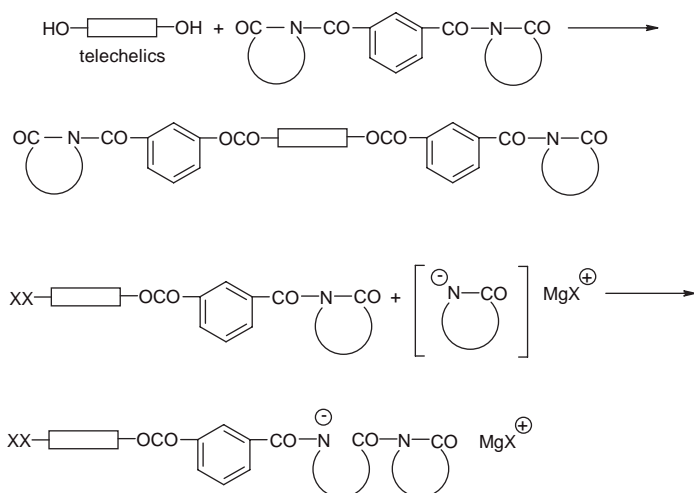
7.7

Block Copolymers of Lactams

The syntheses and properties of block copolymers (especially of those containing PA 6 as blocks) have been carefully summarized in Ref. [51]. The preparation of copolymers with lactam and nonlactam blocks in the same chain requires the use of a prepolymer that is soluble in the lactam melt (at least 80 °C) and bearing suitable end-groups (OH, NH₂, etc.). The first step of the synthesis is the transformation of end-groups to nonionic growth centers: such a functionalization yields the macroactivator. The growth centers are mostly formed by exchange reactions (solvolysis), or by an addition reaction with diisocyanates; thus, they have the NAL or NCL structure. The second step consists of the polymerization of lactam on these nonionic growth centers [52].

The Nyrim technology was the first successful process to produce block copolymers, namely, poly(ϵ -caprolactam)-*block*-polyether [53]. The OH end-groups of the prepolymer are transformed to the growth centers through an alcoholysis of bis(acyllactams) (Scheme 7.3).

The success of this technology is primarily based on the application of ϵ -caprolactam magnesium bromide (CLMgBr) **29** as initiator. This salt enables the pseudoadiabatic polymerization to proceed at a high rate, and the product to crystallize below the melting point of PA 6. Hence, molding can be completed within several minutes, which is main requirement for RIM processes.



Scheme 7.3 Preparation of block copolymers of lactams: the Nyrim process.

Another group of block copolymers which has been studied is that of poly (ϵ -caprolactam)-*block*-polydiene elastomers. Originally (see Ref. [52]), hydroxy-terminated polybutadienes (PBDs) were functionalized by diisocyanates, mostly by toluene diisocyanate (TDI), **23**. Polymerizations were performed first in solvents for polydienes, such as hexane or decalin [54], and later in the monomer phase [55], but neither the yields nor the mechanical properties of the products proved satisfactory.

Later, with the PCL-*block*-PBD copolymers, effort was focused on optimizing the process—that is, finding a suitable compromise between the content of the elastic phase, the composition of the initiation system, and the final properties. Here, a variety of commercially available aromatic (di)isocyanates and their carbamoyl derivatives were tested [52, 56]. For all materials, the yield of block copolymer was 97% with a total incorporation of PBD to the copolymer structure. However, with increasing PBD concentration the toughness was increased such that an optimum had to be found (for a 10% increase the material toughness was raised by one order of magnitude) because the tensile and flexural characteristics decreased linearly with PBD concentration [52]. Interestingly enough, the mechanical properties could be modified by filling [57]. Block copolymers contain a certain amount of gel which increases with the increasing concentration of elastic segments (70–80%). Crosslinking is most likely caused by a side reaction, and is located in the polyamide matrix rather than in the PBD phase [58].

Similarly, when the PBD block was changed for a polyisoprene block, with varying molar masses (being functionalized by diisocyanates), the result was a marked increase in toughness, accompanied by a drop in modulus and tensile strength [59], which resembled the copolymers with the PBD blocks [52].

An amino-terminated copolymer of butadiene and acrylonitrile (Hycar) was used, with partial success, to modify PA 6 [59]. Distinctively better results were

obtained when CLMgBr **29** and TPBCL **15** were used for the initiation [60]. Under optimum conditions, the yield (up to 95%) was controlled by the concentration of CLMgBr. Logically, the toughness increased markedly with increasing concentration of the elastic phase.

Starting with a functionalization of α,ω -dihydroxy-terminated poly(ethylene oxide) or poly(propylene oxide) by HDI **18**, followed by a reaction with α,ω -diamino-terminated copolymer of butadiene and acrylonitrile, a triblock macroactivator was synthesized; the anionic polymerization of CL at 140°C in the presence of this copolymer gave an A–B–C–B–A copolymer [61]. A similar macroactivator for block copolymer synthesis was prepared by a stepwise anionic polymerization of isoprene (with dilithium α -methylstyrene tetramer) and oxirane [62].

When trifunctional polybutadiene prepared by a radical polymerization was incorporated (to the extent of 2–20 wt%) into the PA 6 matrix at 180°C, using a functionalization by IP **22** and HDI **18** [63], surprisingly, the toughness was markedly increased for a low, built-in PBD concentration of only 2 wt%.

When using decaline as solvent, a macroinitiator based on a hydrogenated PBD was used as a starting substance for block copolymer preparation which was functionalized by bis(carbamoyllactams) under the catalysis of NaH [64].

An elegant assessment of the stability of bonding of the growth center to polymer (i.e. the stability of the macroactivator) was made by following the alcoholysis and aminolysis of *N*-acyllactams and *N*-substituted carbamoyl lactams [65, 66].

7.8

Anionic Copolymerization of ϵ -Caprolactam with ω -Lauro lactam

Currently, research into anionic copolymerization is focused on the pair ϵ -caprolactam (CL)/ ω -lauro lactam (LL)—that is, industrially available lactams. A number of other pairs of lactams have been described [7, 11, 67].

The rate of incorporation of a particular lactam depends on the mutual reactivities of the lactam anions, and of the growth centers derived from individual lactams. Their concentrations are determined by the relative acidities of the comonomers and transamide bonds of the copolymer being formed, by a temporal change of the dielectric constant of the feed in dependence on different consumptions of both monomers, and so on [6].

NaH [68], the sodium or potassium salt of CL [69], C_2H_5MgBr [70] or CLMgBr **29** [71] were most frequently used as initiators of copolymerization. In order to accelerate the process, NAL **11** [70] isocyanates, and *N*-substituted carbamoyl lactams were used [69, 72]. All anionic copolymerizations were performed in the range of 130–180°C; in the initial stage, the copolymer was enriched with CL, which was more reactive. However, the individual data obtained were conflicting and differed in the final amounts of built-in LL.

With activated copolymerizations initiated by CLNa **2**, random copolymers are formed within the whole concentration range of both lactams. The melting

temperature (T_m) of the copolymers depends on the ratio of incorporated comonomers, with the minimum (ca. 135°C) appearing approximately at the equimolar composition of the polymerization feed [73], accompanied by a minimum of the crystalline phase content. Wide-angle X-ray scattering (WAXS) analysis indicated α - or γ -phase in copolymers with a prevailing content of CL or LL, respectively; however, for compositions close to equimolar the α - and γ -phases sometimes coexisted [74]. The lengths of the homogeneous sequences (assessed using ^{13}C NMR) were identical to those of random copolymers obtained by a hydrolytic polymerization [75].

In contrast, the copolymers prepared using CLMgBr at 150–180°C had a heterogeneous character, with between 30 and 70 mol% incorporated CL units, while the copolymer showed two distinctive melting endotherms in the range of 130–140°C and 200–220°C [68]. A detailed kinetic study of an equimolar mixture of CL and LL at 150°C showed that a homopolymer (PA 6) is formed preferentially in the system at the start of the process, while the statistical copolymer was formed later with the slowly reacting LL. The material was fractionated (with boiling ethanol) and, according to ^{13}C NMR spectra, consisted of a statistical 1:1 copolymer of LL and CL (~130°C,) and of block copolymer formed from blocks of statistical CL/LL copolymer and CL homopolymer (130 and 210°C) [76].

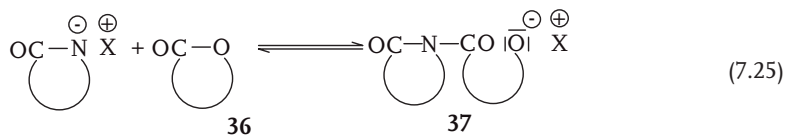
Nevertheless, this process is not exceptional for CLMgBr **29**. For temperatures below 120°C, the copolymerization with CLNa yields also a mixture of random and block copolymers, whereas at higher temperatures the CLNa catalyzed a rapid randomization of the system.

The differences between initiators are given by different participation of the propagation, transamidation (base-catalyzed) and side reactions that depend predominantly on temperature, concentration, the type of initiator, the type and character of the growth centers, and by the complex ionic equilibrium, including the dissociation, association, change of the permittivity of the reaction medium, and so on.

7.9

Copolymerization of Lactams with Lactones (ϵ -Caprolactone)

According to Section 7.4, the activation of the polymerization of lactams by ϵ -caprolactone **36** (CLO) is efficient, but at higher concentration of the later polyester-amide copolymers are produced. In fact, this is a rare example of the copolymerization of cycles that have different mechanisms of the formation of the homopolymers and give rise to a copolymer. The initiation step is the acylation of lactone by the lactam anion [38, 77].



In theory, this structure of the growth center **37** offers the possibility of obtaining a block copolymer, although polyester chains from lactone are formed immediately on the alkoxide anion (as early as during preparation of the polymerization feed) [77], whereas the lactam monomer is built-in more slowly, by an order of magnitude. As shown previously [40], the growth centers for the incorporation of CL arise afterwards, from the poly(ϵ -caprolactone) chains. Although, only a small percentage of ester groups (from CLO **36**) is responsible for the formation of the growth centers, at high conversion the copolymer has a random structure and a high molar mass [40], irrespective of the type of initiator used (whether CLNa (NaH, Na), LiAlH(OC(CH₃)₃)₃ or CLMgBr). Therefore, in addition to the propagation reaction, the transacylation reactions must also proceed, which lead to a randomization of the product.



Transreactions are undoubtedly base-catalyzed, and their rates must be comparable with that of the propagation. The statistical character of the copolymer is supported not only by a single melting temperature, but also by IR and NMR spectra and X-ray analysis [77].

However, a detailed inspection of the thermal spectra (using thermogravimetric analysis; TGA) suggests that the copolymer contains parts (blocks) which are enriched with the CLO or CL units [78]. An analysis of the NMR spectra of the CL/CLO copolymers, with respect to the content of dyads, also showed a certain deviation from random statistics [79]. For the polymerization casting of copolymers starting from the feed containing CL, poly(ϵ -caprolactone), CLMgBr, and using additional NAL activators, the process could be carried out at an unusually low temperature of 110°C [40]. The copolymerization of CLO with LL was also successful [79], as was the preparation of the CL/LL/CLO terpolymers [80].

It is apparent that a possible preparation of the block copolymers of lactams and a lactone (i.e. CL, LL and CLO) must be kinetically controlled in order to suppress the transamidation and transacylation reactions; a short polymerization time and an intensive stirring must be guaranteed. When α,ω -dihydroxy poly(ϵ -caprolactone), functionalized *ex situ* by diisocyanates (MDI), was used as a starting substance, the gradual charging of this material into the Brabender internal mixer, together with a partially polymerized feed (LL, NaH, AcCL **13**) yielded a copolymer in which longer sequences of ϵ -caprolactone units were present [74].

Similar possibilities and limitations are guaranteed when the polymerization is performed in a twin-screw extruder. If CL or LL—or their mixture, NaH and AcCL **13**—were charged first, and CLO into the second hopper, then block copolymers were obtained, the lengths of which could be controlled by the speed of monomer charging [81].

7.10

Powdered Polyamide

The anionic polymerization of lactams represents the only suitable method to prepare powdered PA materials. One advantage here is that the polymerization process is fast, even at temperatures much below than the melting temperature of the synthesized polyamide. Powdered PAs have a number of applications, including flame spraying, electrostatic coating and paste preparation (mainly for cosmetics).

Polymerization and copolymerization proceed in organic liquids, which act as precipitants for the PA being formed. For this, nonpolar solvents such as xylene, ethylbenzene [82], *n*-heptane [83], various gasoline fractions [83] and oils are generally applied. In most cases, the processes used resemble dispersion polymerization (when the monomer is soluble in the medium), although suspension polymerization (when the lactam is only incompletely soluble in the given medium) may also be used.

In recent years, many of the processes initiated by Synhydride (soluble in non-polar media) and aliphatic or aromatic (di)isocyanates [82], carbodiimides [84] or *N*-lauroyl- ϵ -caprolactam [83] have been studied, although the first initiation system was composed of the sodium salt of CL and CO₂ [85].

The polymerization requires a higher concentration of the initiation system and a different initiator/activator ratio when compared to bulk polymerization. The resultant PA has a high molar mass, and no marked side reactions accompany the polymerization, due mainly to the low polymerization temperatures utilized, which mainly range between 90 and 130 °C [82].

The rate of the isothermal process and the morphology of the particles depend not only on the type of initiation system and temperature, but also on the dispersion medium used, and on the speed of stirring [83]. The stage which seems most decisive for characterizing of the particles is the initial polymerization process; this can be quantified by the time needed for the system to become turbid [84]. Such time is determined by the type—that is, the activity—of the initiator and activator. Crystallization of the polymer is preceded by a separation of the liquid phase containing a substantial amount of the polymer, which is determined by the rate of propagation. If the induction period is short, then the polymer will form granules. If the initiation is the rate-controlling step, then the polymer chains are formed gradually and a powdered polymer is formed. The granules formed are agglomerates, the dimensions of which range between 250 and 500 μ m. These can be disintegrated by milling to produce compact particles of 2 to 20 μ m in size [86]. Whilst the above considerations and conclusions are valid for a constant experimental procedure of the process, the formation of particles can clearly be influenced by the dosing of the components to the initiation system.

A very rapid initiation system—namely, a combination of the sodium salt of CL and cyclohexyl isocyanate [87]—made it possible to shorten the polymerization times to 10 min (at 155 °C). The polyisobutylene (PIB) oils used partially dissolved

the CL and, consequently, the yields and particle size (50–500 μm) were determined also by the molar mass of the PIB oil.

In a recent patent, a preparation of powdered PA 12 by dispersion polymerization in hydrocarbon solvents was described where the polymerization mixture contained, in addition to the initiation system, a mineral filler and bisamide [88]. Powdered polyester-amides were prepared in a similar way, namely by the copolymerization of a lactam and a lactone [89].

7.11

Nanocomposites

Polyamide/layered silicate nanocomposites with improved mechanical properties can in general be prepared in three ways: (i) *in situ* polymerization; (ii) mixing in melt; or (iii) exfoliation–adsorption. A successful research study initiated during the 1980s by Toyota Co. focused on a polymerization of ϵ -caprolactam by a hydrolytic mechanism in the presence of an organically modified montmorillonite (MMT): sodium ions present in the interlayers of MMT were substituted by protonated ω -aminolauric acid [90, 91]. ϵ -Caprolactam, ϵ -aminocaproic acid and H_3PO_4 were then added to a dispersion of MMT in water such that, when the polymerization had been carried out, a fully exfoliated morphology of MMT was produced.

To date, no completely successful preparation of nanocomposites using an anionic polymerization of CL in the presence of organophilized MMT has been described in the specialist literature. During the anionic polymerization, alkylammonium cations present in the interlayer of the organophilized MMT are substituted by the counteranions of the lactam anion; this leads to a decrease in the interlayer distance [92], which in turn hampers the penetration of monomer molecules between the silicate platelets.

Recently, nanocomposites were prepared by the anionic polymerization of ϵ -caprolactam using an unmodified MMT [93]. Due to interactions between the water molecules and the polar groups of MMT in the presence of CL, a delamination of the platelets of MMT takes place, thus allowing a stable dispersion MMT-CL- H_2O to be prepared. The water and part of the CL are then distilled off from the mixture. Subsequent X-ray diffractometry (DRX) analysis confirmed a full exfoliation of the Na^+MMT in CL in this intermediate. The next step in the process is to introduce an activator (TDI–23) and an initiator (sodium salt of ϵ -caprolactam). The nanocomposite thus obtained had an exfoliated structure.

7.12

Anionic Polymerization of 2-Pyrrolidone

The polymerization of 2-pyrrolidone (PD) differs markedly from that of CL, mainly because PD can be transformed into a homopolymer only by anionic polymerization.

A low ceiling temperature of the PD polymerization ($\sim 70^\circ\text{C}$) makes it possible to carry out the polymerization at low temperatures only [94, 95].

In general, alkali salts of lactams or suitable nucleophilic agents (e.g. KOH, potassium *tert*-butoxide or complex hydrides) are mainly used as initiators of the PD anionic polymerization. Similar to the CL polymerization [96], the counterions affect polymerization activity and a similar sequence in their efficiency was identified [97].

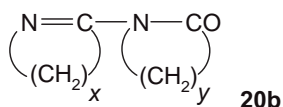
In order to accelerate the polymerization of PD, mainly *N*-acyl-2-pyrrolidone activators (*N*-acetyl-2-pyrrolidone [98], *N*-benzoyl-2-pyrrolidone [99, 100] or *N,N'*-adipoyldi-2-pyrrolidone) were used, although the activity of γ -butyrolactone was also studied [101]. An activated anionic polymerization of PD proceeds optimally in the temperature range of $40\text{--}50^\circ\text{C}$ [100, 102], for a few minutes at most in the homogeneous system, because the rate of propagation markedly exceeds the rate of nucleation and crystallization of polymer. At this stage, which is decisive for the further course of the polymerization [103, 104], a substantial part of the transformation of monomer to a low-molar-mass polymer is carried out ($\sim 40\%$). A limit conversion is achieved during the following slow, heterogeneous stage, but this takes tens of hours.

At the polymerization temperatures applied, salts of 2-pyrrolidone are not fully dissociated. However, an enhancement of the dissociation, and thus a marked increase in polymerization rate, can be achieved by an addition of crown ethers [105].

In a nonactivated polymerization, which is an order of magnitude slower from the outset, the polymerization of PD runs as a heterogeneous process, with its conversion–time dependences being linear at least up to 50% conversion (formal zero-order kinetics) [106]. The high values of molar mass that are attained in this way confirm a low concentration of the growth centers. The polymers prepared by nonactivated polymerization contain no labile structures, which otherwise arise from side reactions [107], and also show a better thermal stability than those synthesized by activated polymerization [108]; this should be true also for the CL polymerization.

An anionic polymerization of PD, accelerated by CO_2 or by potassium 2-pyrrolidone carboxylate, represents a special case [34] that enables the preparation of a relatively thermally stable polymer with a high molar mass. Its kinetics resembles that of the nonactivated polymerization [109, 110].

N-Iminolactams (NIL), which were mentioned briefly in the case of CL polymerizations, and are prepared via a reaction of lactams with lactimethers **20b** [111], show a similar effect as CO_2 but accelerate the polymerization process to a much greater degree:



$x = y = 3$ 1-(1-pyrrolin-2-yl)-2-pyrrolidone

(PDPPD) **38**

$x = 5, \gamma = 3$ *N*-(1-azacyclohept-1-en-2-yl)-2-pyrrolidone (CLPD) **39**

$x = \gamma = 5$ *N*-(1-azacyclohept-1-en-2-yl)- ϵ -caprolactam (CLCL) **20**

$x = 7, \gamma = 3$ *N*-(1-azacyclonon-1-en-2-yl)-2-pyrrolidone (CYPD) **40**

In the anionic polymerization of PD (30–50 °C), the dependences of conversion, as well as the degree of polymerization on time, show a zero-order kinetics up to the 50% conversion [112]. The rate of polymerization decreases in the order CLPD > CYPD > PDPD > CLCL.

In spite of a marked acceleration of the polymerization process due to the presence of NIL, some features of the nonactivated polymerization remain preserved. The growth centers are formed gradually in the polymerization mixture, and the side reactions are also suppressed. A similar reasoning may hold also for the studied polymerization of CL [35].

In order to elucidate the effect of NILs, an isotopically marked 1-(1-pyrrolin-2-yl)-2-[1-¹⁵N]pyrrolidone **38** was prepared. A linear growth of the amount of ¹⁵N PDPD incorporated into the polymer, depending on the polymerization time, testifies that PDPD generates the growth centers at a constant rate [113].

7.13

Summary and Prospects

Whilst polyamides obtained by the ROP of lactams, and preferably of ϵ -caprolactam, are considered to belong to ‘commodity plastics’, their physico-mechanical and chemical properties define them more as ‘construction materials’. The primary advantage of the anionic mechanism (as discussed in this chapter) is that it allows the polymerization of ϵ -caprolactam to be carried out below the melting temperature of the resultant polymer. Since, in the case of PA 6 this leads to a decrease in unreacted monomer content to less than 2 wt% of the product, it is not necessary to further reduce such content by final extraction. A second advantage of the process is the rate at which equilibrium is reached, as this can be adjusted to within a few minutes by using a two-component initiation system.

Understandably, anionic polymerization is less robust than the more widely used hydrolytic ϵ -caprolactam polymerization. It is a sensitive process that requires high-purity components and careful treatment, but allows the preparation of materials with selected or tailored properties. The beauty of the process is its ability to ‘tune’ the polymerization and properties of the polymer product by making only minor changes.

The crucial point of PA formation via the anionic mechanism is that of initiation, as this governs the process as a whole; in this way, the system can be modified to extend its properties for other purposes. Indeed, this area will undoubtedly form the basis of future research topics in the preparation and application of new, special materials.

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8

Ring-Opening Metathesis Polymerization

Michael R. Buchmeiser

8.1

General Introduction

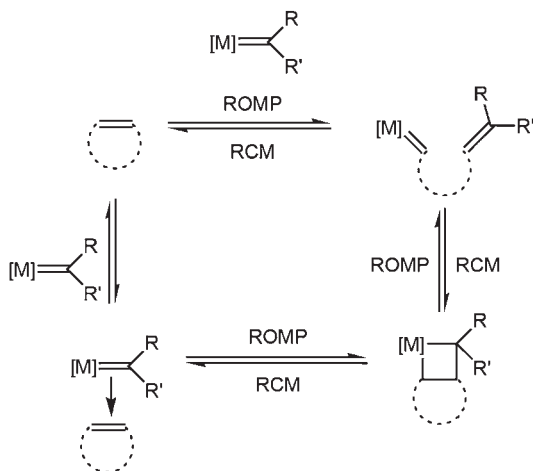
A few years ago, an excellent compilation of all aspects of metathesis chemistry, including those of ring-opening metathesis polymerization (ROMP), was edited by R. H. Grubbs [1]. In this chapter, the basic principles of ROMP—as well as the particular features of the most important initiators relevant to ROMP—are outlined. In view of the quite comprehensive set of data reported in the above-mentioned book, and the limitations in space in this chapter, only the latest relevant developments in ROMP will be summarized at this point.

8.2

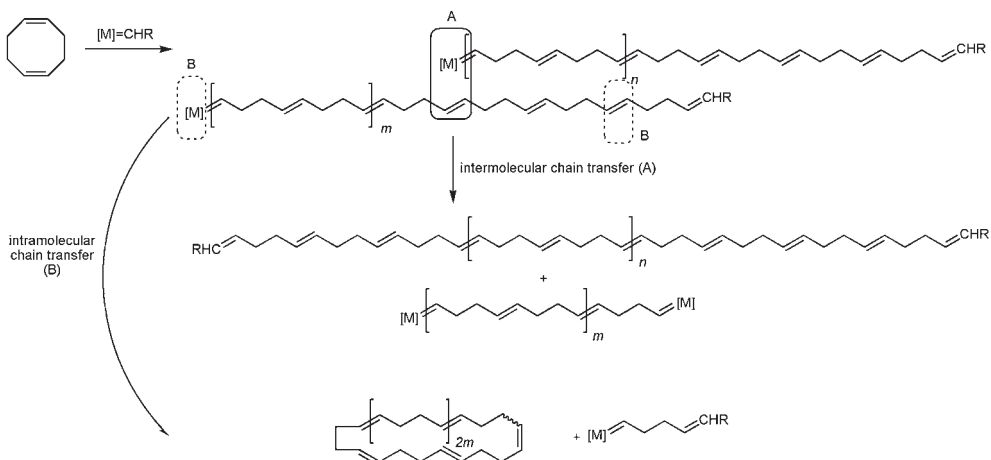
Introduction to Ring-Opening Metathesis Polymerization (ROMP)

Ring-opening metathesis polymerization is a transition metal alkylidene-triggered process in which cyclic olefins, whether mono-, bi- or multicyclic, undergo ring opening and are concomitantly joined together to form a polymer chain. ROMP is thus a chain-growth polymerization and belongs, together with Ziegler–Natta-type polymerizations and group transfer polymerizations, to the family of polyinsertions. The mechanism is based on olefin metathesis [2–5]. The ring-opening process occurs at the most stable site of the monomer—that is, the double bond—a finding that turned early discussions about the mechanism of this polymerization technique into a quite vivid affair [6]! The basic process of ROMP is shown in Scheme 8.1.

It is important to note that, as with all metathesis reactions, all of the steps are—in principle—reversible, and consequently ROMP may be regarded as an inversed ring-closing metathesis (RCM) reaction. ROMP is driven by the thermodynamics that are entailed with the reduction in ring-strain that occurs during incorporation of the monomer into the growing chain. In general, the ring opening of three-, four-, eight- and larger-membered rings is energetically favored [7]. The



Scheme 8.1 The ROMP process in schematic form.



Scheme 8.2 Intermolecular (A) and intramolecular (B) chain-transfer reactions in ROMP.

overall value of ΔG for the ROMP process of seven-membered rings (and in particular of five- and six-membered rings)—that is, whether positive or negative—depends heavily on the concentration of the monomer, the substituents at the ring, and the fact whether the cyclic olefins are part of a bi- or multicyclic ring system. A more detailed discussion, including values for ΔH° , ΔS° and ΔG° for the ROMP of selected cyclic olefins can be found in Ref. [8]. Finally, as the polymer itself still contains double bonds (i.e. one per repeat unit), an intramolecular chain-transfer reaction (a back-biting process) may also occur, leading to cyclic oligomers/polymers (Scheme 8.2) [9–12].

The extent of this process depends heavily on temperature, monomer concentration, the *cis/trans* configuration of the double bonds within the polymer backbone,

the solvent, reaction time and—perhaps most importantly—on the steric bulk of the monomer used.

8.3

Well-Defined Catalysts for ROMP

The fact that ROMP holds nowadays such a strong position in polymer chemistry is certainly a consequence of the developments in catalyst or, in the context of polymerizations, initiator design. Numerous groups have contributed to that area [8, 13–23], and an excellent summary of these studies is provided elsewhere [1, 24]. However, among the large number of important contributions, the studies of two groups deserve particular attention—as recognized by the award of the 2005 Nobel Prize for chemistry to R.H. Grubbs [1, 25–27] and R.R. Schrock [28–33]. The award was shared with Y. Chauvin [6], who was honored for his fundamental studies on metathesis. The investigations of Grubbs and Schrock led to the development of well-defined transition metal alkylidenes that rapidly outrivalled any other initiator or initiation system, particularly those consisting of an often serendipitous mixture of transition metal salts, alcohols and tin alkyls. Some examples of Grubbs- and Schrock-type initiators are shown in Figure 8.1.

These initiators have the advantage of being well-defined compounds, and in particular of possessing preformed metal-alkylidenes. Their development, synthesis and properties will be outlined here in more detail.

8.3.1

Schrock-Type Initiators

The synthesis of well-defined, high-oxidation state molybdenum alkylidenes was first reported by Schrock and coworkers in 1990 [34]. These, and the analogous tungsten systems, are now commonly named ‘Schrock-catalysts’. The systems possess the general formula $M(\text{NAr}')(\text{OR}')_2(\text{CHR})\text{L}$, where $M = \text{Mo}, \text{W}$; $\text{Ar}' = \text{phenyl}$ or a substituted phenyl group; $\text{R} = \text{ethyl}, \text{phenyl}, \text{trimethylsilyl}, \text{CMe}_2\text{Ph}$ or *t*-butyl; $\text{R}' = \text{CMe}_3, \text{CMe}_2\text{CF}_3, \text{CMe}(\text{CF}_3)_2, \text{C}(\text{CF}_3)_2$, aryl, and so on, while $\text{L} = \text{quinuclidine}, \text{trialkylphosphane}$ and tetrahydrofuran (THF). The most commonly used (and also commercially available) systems are based on the

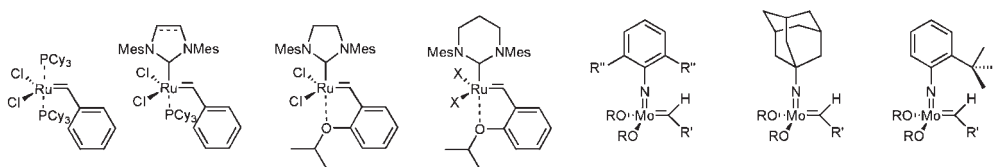
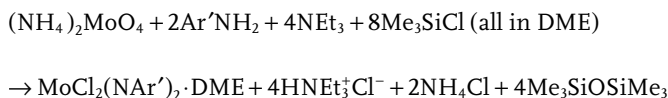


Figure 8.1 Selected examples of Grubbs- and Schrock-type initiators. $\text{X} = \text{Cl}, \text{CF}_3\text{COO}$, $\text{R} = \text{C}(\text{CH}_3)_3, \text{C}(\text{CH}_3)(\text{CF}_3)_2$; $\text{R}' = \text{C}(\text{CH}_3)_2\text{Ph}, \text{C}(\text{CH}_3)_3$; $\text{R}'' = \text{CH}_3, 2\text{-Pr}, \text{Cl}$.

neopentylidene, neophylidene, the 2,6-(2-Pr)₂-C₆H₃-imido and the *t*-butoxide, hexafluoro-*t*-butoxide and the (substituted) binaphtholate and biphenolate ligand. The formation of MoCl₂(NAr')₂·DME is conveniently accomplished via the reaction of ammonium molybdates [35] or sodium molybdate with the corresponding aniline (amine) in the presence of an auxiliary amine (triethylamine) and trimethylchlorosilane [36]. The entire reaction, which may be conducted in dimethoxyethane (DME) in virtually quantitative yields, is described by the following stoichiometry:

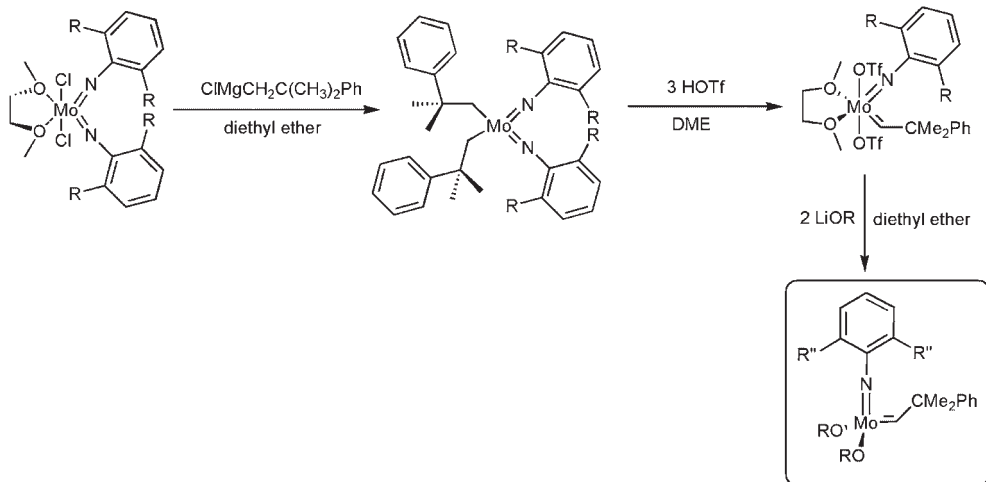


where Ar' is a substituted aryl group. Although a wide variety of arylamines may be used, the use of the corresponding alkyl-analogue is more or less restricted to sterically demanding amines such as *t*-butyl amine. The use of aliphatic amines bearing electron-withdrawing groups, for example of hexafluoro-*t*-butylamine, allows only for the synthesis of molybdenum mono-oxomonoimido chloride complexes [37]. Molybdenum bisimidodichlorides of the general formula MoCl₂(NAr')₂·DME react smoothly with Grignard reagents such as neophyl- or neopentylmagnesium chloride to yield the corresponding molybdenum bisimidodialkyl complexes Mo(NAr')₂(CH₂R). Consecutive reaction with 3 equiv. of triflic acid (HOTf) in DME yields the molybdenumimidoalkylidene bistriflates Mo(NAr')(OTf)₂(CHR)·DME, which may then be transformed into a large variety of different Schrock-type catalysts of the general formula Mo(NAr')(OR')₂(CHR) by reaction with 2 equiv. of a lithium alkoxide LiOR' [38]. A broad variety of alkoxides such as *t*-butoxide, trifluoro-*t*-butoxide, hexafluoro-*t*-butoxide, perfluoro-*t*-butoxide, phenoxides and substituted binaphtholates may be used for these purposes. A summary of the entire reaction pathway is provided in Scheme 8.3.

8.3.2

Grubbs-Type Initiators

In 1992, Grubbs *et al.* described the synthesis of the first well-defined ruthenium alkylidene [39, 40]. Thus, the reaction of RuCl₂(PPh₃)₃ and RuCl₂(PPh₃)₄, respectively, with 2,2-diphenylcyclopropene in benzene or methylene chloride yielded the desired ruthenium carbene complex RuCl₂(PPh₃)₂(CH=CH=CPh₂). As is the case of Schrock-type catalysts, the alkylidene proton in RuCl₂(PPh₃)₂(CH=CH=CPh₂) experiences an agostic interaction with the metal, resulting in downfield NMR shifts for H_α and C_α to δ = 17.94 and 288.9 ppm, respectively (both in C₆D₆). Despite a ratio of *k_i*/*k_p* < 1 (*k_p* = rate constant of polymerization, *k_i* = rate constant of initiation), the compound was found to be a quite efficient initiator for the polymerization of norbornene (NBE) and substituted NBEs. The comparably low activity of the bis(triphenylphosphane)-derivative for other cyclic olefins than NBE



Scheme 8.3 The synthesis of Schrock catalysts. $\text{R} = \text{C}(\text{CH}_3)_3$, $\text{C}(\text{CH}_3)(\text{CF}_3)_2$; $\text{R}'' = \text{CH}_3$, 2-Pr, Cl: $\text{Tf} = \text{CF}_3\text{SO}_2$.

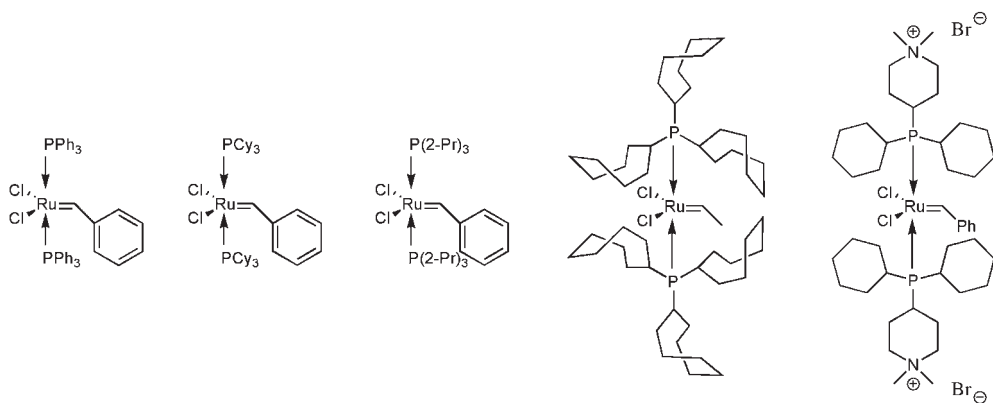
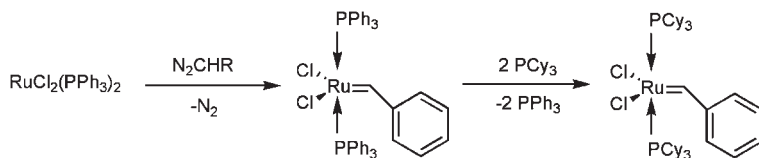


Figure 8.2 A selection of 'first-generation' Grubbs-type initiators.

such as bicyclo [3.2.0]hept-6-ene or *trans*-cyclo-octene was successfully enhanced by phosphane exchange with more basic analogues, for example tricyclohexylphosphane and tri-(2-propyl)phosphane (Figure 8.2) [40].

An alternative route to ruthenium alkylidenes that avoided the preparation of 2,2-diphenylcyclopropene was elaborated by Schwab and Grubbs [41, 42]. The synthetic protocol entailed the reaction of $\text{RuCl}_2(\text{PPh}_3)_3$ with an diazoalkane (Scheme 8.4).

Via this route, the resulting compounds of the general formula $\text{RuCl}_2(\text{PR}_3)_2(\text{CHPh})$, ($\text{R} = \text{Ph}$, Cy_3)—which today are well known as the first-generation Grubbs catalyst—are accessible in high yields. Phosphane-exchange from the parent bis(triphenylphosphane) systems into the more reactive bis(tricyclohexylphosphanes) may be performed either consecutively or *in situ*. The reaction of



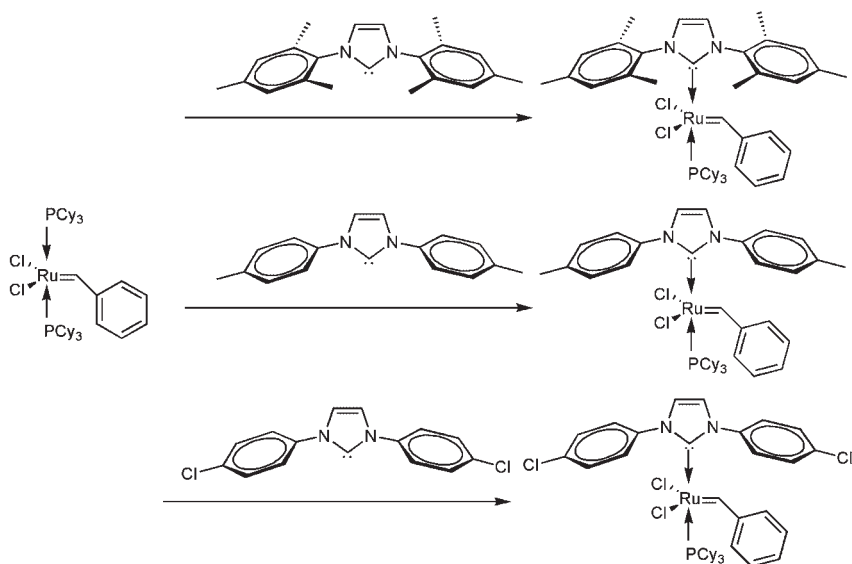
Scheme 8.4 Grubbs catalyst synthesis.

diazo-compounds with ruthenium arene complexes has also been used for the *in situ* generation of ruthenium alkylidenes from $[\text{RuCl}_2(p\text{-cymene})]_2$, tricyclohexylphosphane and trimethylsilyldiazomethane [43]. The synthesis of entirely water-soluble analogues was accomplished by the use of phosphanes containing quaternary ammonium groups (Figure 8.2) [44, 45]. These water-soluble systems have also been investigated in terms of their stability versus Brønsted acids, such as DCl [46]. Interestingly enough, and in contrast to the behavior of ‘classical’ water-soluble systems such as $\text{RuCl}_2 \cdot x\text{H}_2\text{O}$, the addition of an acid did *not* interfere with the ruthenium alkylidene, but effectively protonated one phosphane group, thus generating a more active monophosphane complex. The corresponding monophosphane adducts were found to be stable and quantitatively initiated ROMP of cyclic olefins. Interestingly, the same monophosphane-adducts were suggested to be the active species in the ROMP in the gas phase [47]. The resulting initiators were again found to polymerize 2,3-difunctionalized norbornadienes and their 7-oxa-analogues, with high *trans*-stereoselectivity [48, 49].

A synthetic protocol consisting of the reaction of $\text{RuCl}_2(\text{PPh}_3)_2(\text{CHR})$ with imidazol-2-ylidenes [50–52] was used for the generation of another type of ruthenium-based system. While bis(N-heterocyclic carbene) complexes displayed a comparably low reactivity in ROMP [18, 19], the corresponding mono-N-heterocyclic carbene–monophosphane complexes turned out to be highly active [18, 19, 53].

In this context, 1,3-bis(2,4,6-trimethylphenyl)imidazol-2-ylidene (IMes), 1,3-bis(4-methylphenyl)imidazol-2-ylidene (ITol) and 1,3-bis(4-chlorophenyl)imidazol-2-ylidene (IpCl) were successfully used for the preparation of mixed-ligand ruthenium carbenes of the general formula $\text{RuCl}_2(\text{PR}_3)(\text{IMes})(\text{CHPh})$, ($\text{R} = \text{Cy}, \text{Ph}$), [53, 54], $\text{RuCl}_2(\text{PR}_3)(\text{IMes})(\text{CHCHCPh}_2)$, $\text{RuCl}_2(\text{PR}_3)(\text{ITol})(\text{CHPh})$ and $\text{RuCl}_2(\text{PR}_3)(\text{IpCl})(\text{CHPh})$ [54] (Scheme 8.5). Changing from the IMes to the 1,3-dimesityl-4,5-dihydroimidazolin-2-ylidene (IMesH₂) ligand again significantly increased the activity of the catalyst [55–57]. The corresponding catalyst, $\text{RuCl}_2(\text{PCy}_3)(\text{IMesH}_2)(\text{CHPh})$ is today known as the second-generation Grubbs catalyst (Figure 8.3). Another breakthrough in catalyst activity was the development of Grubbs-type initiators with an internally oxygen-chelated ruthenium alkylidene (Figure 8.3).

Thus, the reaction of $\text{RuCl}_2(\text{PPh}_3)_2$ with 2-(2-propoxy)phenyldiazomethane leads to the formation of $\text{RuCl}_2(\text{PCy}_3)(\text{CH-2-(2-PrO)-C}_6\text{H}_4)$. Alternatively, this compound—which turned out to be highly stable and even chromatographically recyclable—may be prepared by the reaction of $\text{RuCl}_2(\text{PCy}_3)_2(\text{CHPh})$ with



Scheme 8.5 Synthesis of selected Ru^{IV} -N-heterocyclic carbene complexes.

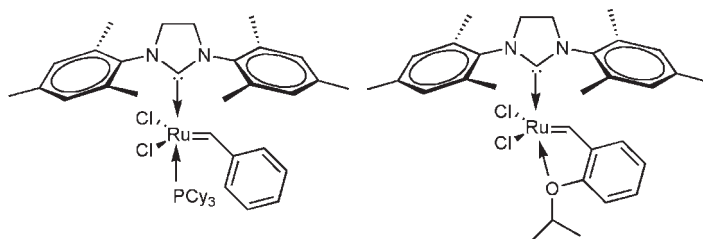
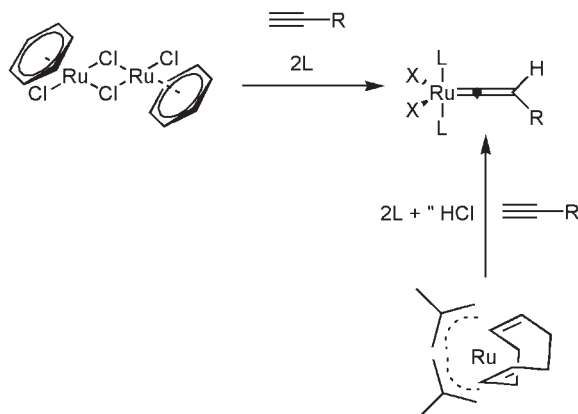


Figure 8.3 Second-generation Grubbs (left) and Grubbs-Hoveyda catalysts (right).

2-(2-propoxy)styrene [16]. Another variation in Grubbs-type catalysts is worthy of mention at this point. Thus, Buchmeiser *et al.* reported on the synthesis of Ru-carboxylate [58] and bis(trifluoroacetate) derivatives of the general formula $\text{Ru}(\text{CF}_3\text{COO})_2(\text{NHC})(\text{CHR})$ and $\text{Ru}(\text{CF}_3\text{COO})_2(\text{PCy}_3)(\text{NHC})(\text{CHPh})$ ($\text{NHC} = \text{IMes}$, IMesH_2 , 1,3-dimesityl-3,4,5,6-tetrahydropyrimidin-2-ylidene; $\text{R} = 2-(2\text{-PrO})\text{-C}_6\text{H}_4$, 2-MeO-5- $\text{NO}_2\text{-C}_6\text{H}_3$) [23, 59–66]. Although their reactivity in ROMP has also been investigated (*vide infra*), a key property of these compounds is their ability to allow for the ('living') cyclopolymerization of 1,6-heptadiynes [67].

Finally, ruthenium vinylidene complexes must be mentioned [68, 69]. Compounds of the general formula $[\text{RuCl}_2(\text{C}=\text{CHR})\text{L}_2]$ ($\text{L} = \text{PPh}_3$, $\text{P}(2\text{-Pr})_3$, PCy_3 , Cp (C_5H_5), Cp^* (C_5Me_5) IMes , IMesH_2) are readily accessible via the reaction of $[\text{RuCl}_2(\text{p-cymene})]_2$ and a terminal alkyne (according to Scheme 8.6), and may well serve as initiators for ROMP.



Scheme 8.6 Exemplary synthesis of Ru-vinylidene complexes ($X = \text{Cl}$).

8.4

'Living' ROMP [70]

As discussed in Chapter 4, the term 'living' polymerization was first introduced into polymer science by Szwarc [71–73] who, while investigating anionic polymerization, elaborated the principles of these particular polymerizations. Today, 'living' polymerizations have been defined by the IUPAC as *'chain polymerizations from which chain-transfer and chain-termination reactions are absent'* (see also Scheme 8.2). As a matter of fact, ROMP may be carried out in a truly 'living' manner with many of the above-mentioned initiators, although the livingness also depends heavily on the monomer used. If successfully established, 'living' systems allow for the synthesis of (multi-)block copolymers. Although metathesis reactions (including ROMP) are all equilibrium reactions, the polymerization of cyclic olefins with high ring strain is thermodynamically favored, thus providing the irreversibility of each initiation step that is required in establishing the desired 'living' polymerization set-up. In any case, a 'living' polymerization is not immortal, and therefore at a certain period of time chain-termination or chain-transfer reactions may well be observed. Matyjaszewski suggested a 'ranking' of 'living' systems within six different classes [74]. Class I describes 'living' systems, which are stable for 1 s in the absence of monomer, while class VI systems entail those that are stable for at least 24 h in the absence of any monomer. Although class I–III systems are certainly 'living' systems with low practical relevance, this ranking allows for an additional useful characterization of polymerization systems. Additional useful properties of a 'living' polymerization system include the complete and rapid initiation of the polymerization process, during which course the entire initiator is consumed. 'Rapid' means that the rate constant of initiation, k_i , should be significantly larger than the rate constant of propagation, k_p . If this is the case, then the molecular weight of the polymer may simply be predetermined by the monomer over catalyst ratio. The typical characteristics of 'living' polymerizations

are a linear dependence of molecular weight on monomer conversion, a narrow polydispersity index (PDI; $PDI = M_w/M_n$), and the complete consumption of monomer. The molecular weight distribution of an ideal 'living' polymerization is characterized by a Poisson distribution ($PDI = 1 + 1/P_n$, where P_n is the average degree of polymerization).

8.4.1

ROMP with Schrock Initiators

Generally speaking, Schrock initiators are highly active in the ROMP of a vast variety of cyclic alkenes such as substituted norbornenes, norbornadienes, 7-oxanorbornenes, cyclooctatetraenes (COTs) and cyclooctadienes (CODs) [28], or polycyclic alkenes such as certain quadricyclanes [75]. In addition, they may be used for 1-alkyne polymerization and the cyclopolymerization of 1,6-heptadiynes [67, 76]. Despite the fact that they are highly sensitive towards traces of oxygen or moisture, they possess a remarkable stability versus various functionalities including cyano groups, esters, anhydrides, amides, ethers and amines [77–79]. Binuclear molybdenum alkylidenes have been obtained by reaction of a Schrock carbene with α,ω -dienes such as divinylbenzene or with octatetraene [80]. Such binuclear initiators have recently again been used for the synthesis of various ABA triblock copolymers [81–83].

Schrock-type initiators of the type $Mo(NAr')(OR')_2(ChCMe_2R)$ possess a tetrahedral geometry. The addition of phosphanes such as PMe_3 or amines such as quinuclidine to $Mo(NAr)(OCMe(CF_3)_2)(CH-t-Bu)$ allows (in analogy to W-based systems [84]) the observation and isolation of two isomeric adducts [85]. The attack of the ligand was found to occur preferably at the CNO-face [86], a fact which is in accordance with calculations carried out for the attack of an alkene on such systems [87]. Therefore, the approach of a (bulky) alkene via the CNO face of the initiator is regarded to be the main (if not the only) reaction pathway. The one compound, in which the *t*-butyl or CMe_2Ph group points towards the imido-ligand is commonly called the *syn*-rotamer, while the second with the *t*-butyl group pointing away from the imido ligand is called the *anti*-rotamer (Figure 8.4).

These two rotamers, the reactivity and relative ratio of which is governed by the electronic nature of the alkoxide ligand, were found to be responsible for the structure of the final polymer if used in ROMP. In-depth investigations on the reactivity of these rotamers were carried out in order to shed some light onto

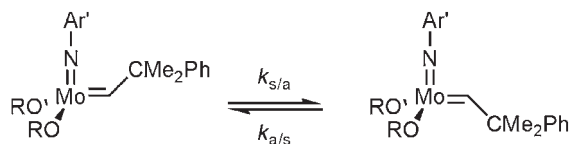
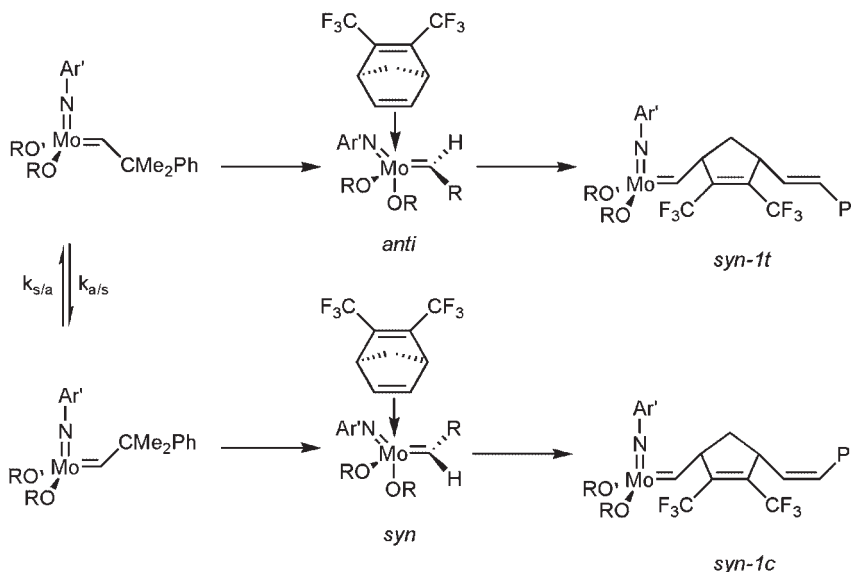


Figure 8.4 *Syn*- and *anti*-rotamers of a Schrock catalyst. $k_{s/a}$ and $k_{a/s}$ are the rate constants for the interconversion of the *syn*- into the *anti*-rotamer, and vice versa.

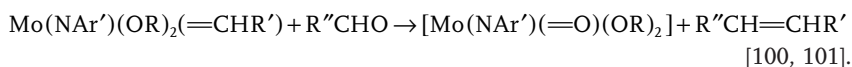
the mechanism responsible for the formation of polymers with high *cis*- or *trans*-vinylene contents. Upon photolysis of a large variety of Mo-based Schrock-carbenes in different coordinating and noncoordinating solvents (toluene, THF), photostationary *syn-anti* mixtures containing up to 35% of the *anti*-rotamer were obtained [88]. Taking advantage of the different chemical shifts of the H_{α} -alkylidene resonances in both isomers (characterized by α -agostic interactions with the Mo-core and typically found between 11 and 13 ppm), the first-order rates of conversion of the *anti*-rotamer to the *syn*-rotamer were determined using 1H -NMR spectroscopy. These investigations revealed that the rate of interconversion depended heavily on the alkoxide. Thus, $k_{a/s}$ was 10^8 -fold higher in $Mo(NAr')(OR)_2(CHR')$ if $R = t$ -butoxide than in the case where $R = CMe(CF_3)_2$. A comparison of these data obtained in toluene with those obtained in THF revealed a decrease for both $k_{a/s}$ and $k_{s/a}$ which was even more pronounced in the case of more electron-withdrawing alkoxides such as $OCMe(CF_3)_2$. These findings were consistent with the expected stronger binding of THF by a more electrophilic metal core, along with the fact that a coordinating ligand must be lost from a five-coordinate species in order to allow interconversion [85]. Also within this context, it is not surprising that 7-oxanorbornadiene-derivatives were found to form observable and even isolable molybdacyclobutanes [89]. Self-consistent field- X_{α} -scattered wave (SCF- X_{α} -SW) calculations were carried out on simplified analogues [$Mo(NH)(OH)_2(CH_2)$], and confirmed the contribution of the alkoxide oxygen 2p orbitals to most other orbitals [90]. Consequently, their influence on the *syn/anti*-interconversion and reactivity of these complexes [91] was obvious. In contrast to 'living' polymerizations carried out with Mo-bis(hexafluoro-*t*-butoxide)-based initiators (which were found to yield all-*cis* polymers with only 75% tacticity [91]), the 'living' polymerizations which resulted from Mo-bis(*t*-butoxide)-derived initiators led to the formation of all-*trans*, highly tactic polymers [92]. The tacticity of such polymers was suggested to be controlled by the chirality of the alkylidenes β -carbon (chain-end control). Thus, among both rotamers of the Mo-initiator $Mo(NAr')(OCMe(CF_3)_2)_2(CHR)$, the *anti*-rotamer was seen to be the more reactive in the reaction with bis(trifluoromethyl)norbornadiene (NBDF6), leading to a *syn*-first insertion product. The configuration of the double bond was determined as *trans* (*anti* \rightarrow *syn*, *trans*). In contrast, the *syn*-rotamer produced a *syn*-first insertion product with a *cis*-configured double bond (*syn* \rightarrow *syn*, *cis*) (Scheme 8.7) [93].

As very little of the *anti*-form is present under equilibrium conditions (without irradiation) in $Mo(NAr')(OCMe(CF_3)_2)_2(CHR)$, and the *syn*- to *anti*-conversion is slow (ca. $10^{-5} s^{-1}$), the *cis*-polymers were proposed to be formed from the *syn*-species of a catalyst via olefin attack on the CNO-face of the initiator [87]. In a *t*-butoxide system, where interconversion is relatively fast (ca. $1 s^{-1}$), it was proposed that the *anti*-form was the only propagating alkylidene species. This proposal was further supported by studies carried out by Feast and coworkers [94]. Using highly unreactive monomers such as 1,7,7-trimethylnorbornene, only the reaction of the *anti*-rotamer at a very slow monomer concentration-independent rate was observed. Additionally, the calculated rate constant was essentially identical with that for the *syn-anti*-conversion. The high dependency of the *cis-trans*-contents of a polymer on the temperature, as was found for the polymerization of 2,3-



Scheme 8.7 Formation of poly(2,3-bis(trifluoromethyl) norbornadiene) with an all-*cis*- and all-*trans*- base from the *syn*- and *anti*-rotamers of a Schrock catalyst.

bis(trifluoromethyl)norbornadiene (NBDF6) with $\text{Mo}(\text{N}-2\text{-}t\text{-BuC}_6\text{H}_4)((2,2'\text{-}[4,4', 6,6'\text{-}t\text{-Bu}_4(\text{C}_6\text{H}_2)_2\text{O}_2])(\text{CHCMe}_2\text{Ph})$, again underlined the importance of *syn-anti*-conversion with respect to the time-scale of the polymerization [95]. Thus, the careful choice of an alkoxide in these systems offers an attractive access to polymers with either *cis*- or *trans*-configured double bonds, as well as to highly tactic polymers [96]. In order to be capable of preparing polymers which are >99% *cis* and >99% tactic, the use of chiral alkoxide ligands was elaborated [97–99]. Finally, it should be mentioned that polymerizations initiated by Schrock-type initiators are best terminated in a Wittig-type reaction by the use of aldehydes, for example benzaldehyde [28] or ferrocenyl carbaldehyde according to the equation:

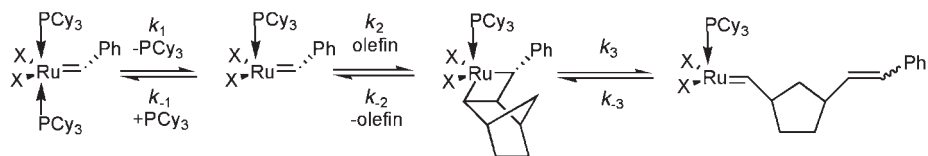


More detailed discussions are available in Refs [24, 29–33, 86, 102].

8.4.2

ROMP with Grubbs-Type Initiators

Compared to molybdenum- or tungsten-based Schrock catalysts, the reactivity of ruthenium-based Grubbs catalysts is somewhat different. Reactivity in $\text{RuCl}_2(\text{PR}_3)_2(\text{CHPh})$ may efficiently be tuned rather via the use of different phosphanes [103] than by the nature of the alkylidene moiety [42] or by substitution of the chlorides by other, more electron-withdrawing groups [104]. In principle, two



Scheme 8.8 Mechanism of ROMP initiated by Grubbs-type initiators.

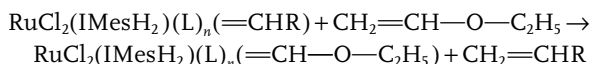
different mechanisms have initially been postulated for ROMP. An associative mechanism, with both phosphanes on the metal center, and a dissociative mechanism, with only one phosphane attached to the ruthenium core. The first translates into an 18-electron transition state, while the latter corresponds to a 16-electron transition state. Interestingly, both mechanisms and the existence of both mono- and diphosphane adducts, respectively, were confirmed with quantum molecular dynamics studies [105]. These studies also confirmed the importance of the use of sterically crowded phosphanes for the preparation of highly active ruthenium alkylidenes, as they lead to longer and consequently less stable Ru–P bonds. However, only the dissociative mechanism was further supported by two findings: (i) the addition of CuCl as a phosphane scavenger resulted in significantly elevated catalytic activity; and (ii) the addition of excess phosphane resulted in a decrease in activity both of RCM and ROMP. The currently accepted mechanism [1, 106, 107] is shown in Scheme 8.8, although it should be mentioned that, very recently, an associative mechanism has again been reported for $\text{RuCl}_2(\text{PR}_3)(\text{IMesH}_2)(\text{CHPh})$ -type initiators ($\text{R} = \text{CH}_3$, butyl) [108].

Piers *et al.* were able to characterize a 14-electron ruthenacyclobutane obtained from the reaction of $[\text{RuCl}_2(\text{IMesH}_2)(\text{CHPCy}_3)^+ \text{B}(\text{C}_6\text{F}_5)_4^-]$ with ethylene [109]. In view of these data and the results reported by Snapper *et al.* [110], a (flattened) intermediary ruthenacyclobutane *trans* to the phosphane or N-heterocyclic carbene ligand appeared to be the most abundant structure. Recent studies conducted by Grubbs *et al.* supported these data [111], although side-bound structures have also been reported by the same group [112].

The importance of ligand—that is, phosphane size and basicity—on metathesis performance [103, 113] was further demonstrated by the finding that even small changes in the PCy_3 ligand allowed for the fine-tuning of this catalytic system. Thus, use of the $\text{PCy}_2\text{CH}_2\text{SiMe}_3$ ligand allows synthesis of the initiator $\text{RuCl}_2(\text{PCy}_2\text{CH}_2\text{SiMe}_3)_2(\text{CHPh})$, which was found to be highly active in the polymerization of norborn-5-ene-2,3-dicarboximides [114]. Staying within the context of phosphane ligand variation, the thermodynamics and in particular the importance of σ -donation related to the exchange of phosphanes, the influence of electronic as well as steric effects of this type of compounds have been studied in detail [103]. The stability as well as the reactivity order that can be deduced from this is $\text{PPh}_3 < \text{PBz}_3 < \text{PCyPh}_2 < \text{PCy}_2\text{Ph} < \text{P-}i\text{-Bu}_3 < \text{P-}i\text{-Pr}_3 < \text{PCy}_3$. With regards to the variation of the other ligands, an increase in *reactivity* in the order $\text{X} = \text{I} < \text{Br} < \text{Cl}$ and $\text{R} = \text{H} < \text{Ph} < \text{alkyl} < \text{COOR}$ for $\text{RuX}_2(\text{PR}_3)_2(\text{CHR}')$ is observed. In contrast, in terms of *initiation*, an increase in the rate constant of initiation has been observed in the order $\text{X} = \text{Cl} < \text{Br} < \text{I}$, $\text{R}' = \text{H} < \text{Ph} < \text{alkyl} < \text{COOR}$ and $\text{PR}_3 = \text{PCy} < \text{PPh}_3$.

At a first glance, this appears to be contradictory, but in view of the reaction cascade of a dissociative mechanism these data nicely explain the catalytic behavior of the different catalysts in ROMP, as well as the physico-chemical data of ROMP-derived polymers. Thus, the use of second-generation-type catalysts in particular resulted in polymers with comparably broad PDIs and molecular weights way above the calculated values. This was the result of poor initiation efficiencies, which themselves were strongly related to phosphane dissociation and alkene coordination. In this context, second-generation Grubbs-type catalysts display significantly reduced values for k_i compared to the parent first-generation catalysts. Furthermore, k_{-1}/k_2 is by far larger for second-generation than for first-generation catalysts. Numerous theoretically based reports have been made which support these data to a great extent [115–123]. Numerous ways of improving the initiation kinetics of Grubbs-type initiators have been elaborated. The simplest form entails the use of additional free phosphane [124]. As an excess of phosphane does not affect k_1 , which is independent of [phosphane], but lowers k_p by increasing k_{-1} [PR_3] compared to k_2 [olefin], the overall value of k_i/k_p is increased. The other entails the use of other coordinating ligands than phosphanes (*vide infra*).

In terms of polymer structure, the ROMP of norborn-2-enes and norbornadienes using ruthenium-based systems generally results in the formation of polymers that predominantly contain *trans*-vinylene units (*vide infra*). For a detailed discussion on the stereochemistry of ROMP-derived polymers and the determination of tacticity, the reader should refer to the chapter by J.G. Hamilton in Ref. [1], and the references cited therein. Polymerizations initiated by Grubbs-type initiators are best terminated by the use of ethyl vinyl ether, yielding methyldene-terminated polymers according to the equation [25]:



8.5

Selected Recent Applications and Developments

8.5.1

Novel Catalysts for ROMP

Allaert and Verpoort *et al.* reported on Schiff base-substituted Ru^{II} compounds [125] and second-generation Grubbs initiators [126] and their use for the ROMP of cyclooctene [127] and norborn-2-ene [128] (Figure 8.5), although the reactivity was lower than that of the parent, second-generation catalyst.

Berke *et al.* reported on cationic low-valent rhenium dinitrosyl-diphosphane complexes of the general formula $[\text{Re}(\text{PR}_3)_2(\text{NO})_2^+ \text{BAR}_f^-]$ ($\text{R} = \text{Cy}, 2\text{-Pr}$; $\text{BAR}_f^- = \text{tetrakis}(3,5\text{-bis}(\text{trifluoromethyl})\text{phenyl})\text{borate}$) [129]. ROMP activity versus norborn-2-ene, cyclooctene and dicyclopentadiene was confirmed. Wagener *et al.* reported on the synthesis of ethylidene-derivatives of a Grubbs' second-generation

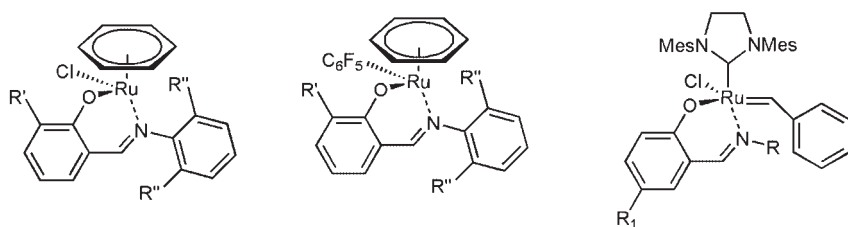
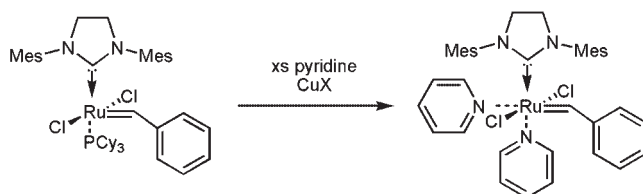


Figure 8.5 Schiff base-substituted Ru^{II} and second-generation Grubbs-type initiators.



Scheme 8.9 Synthesis of a dipyridine analogue of the second-generation Grubbs catalyst.

catalyst for the synthesis of ROMP-derived polymers with linear alkyl chains [130], while Sarkar *et al.* described the ferrocenylmethylidene analogue of Grubbs' first-generation catalyst [131]. Nomura *et al.* reported the first vanadium alkylidene triggered ROMP of norborn-2-ene using $V(N-2,6-Me_2-C_6H_3)((N=C(CMe_3)_2)(CHSiMe_3)(PMe_3))$ [132].

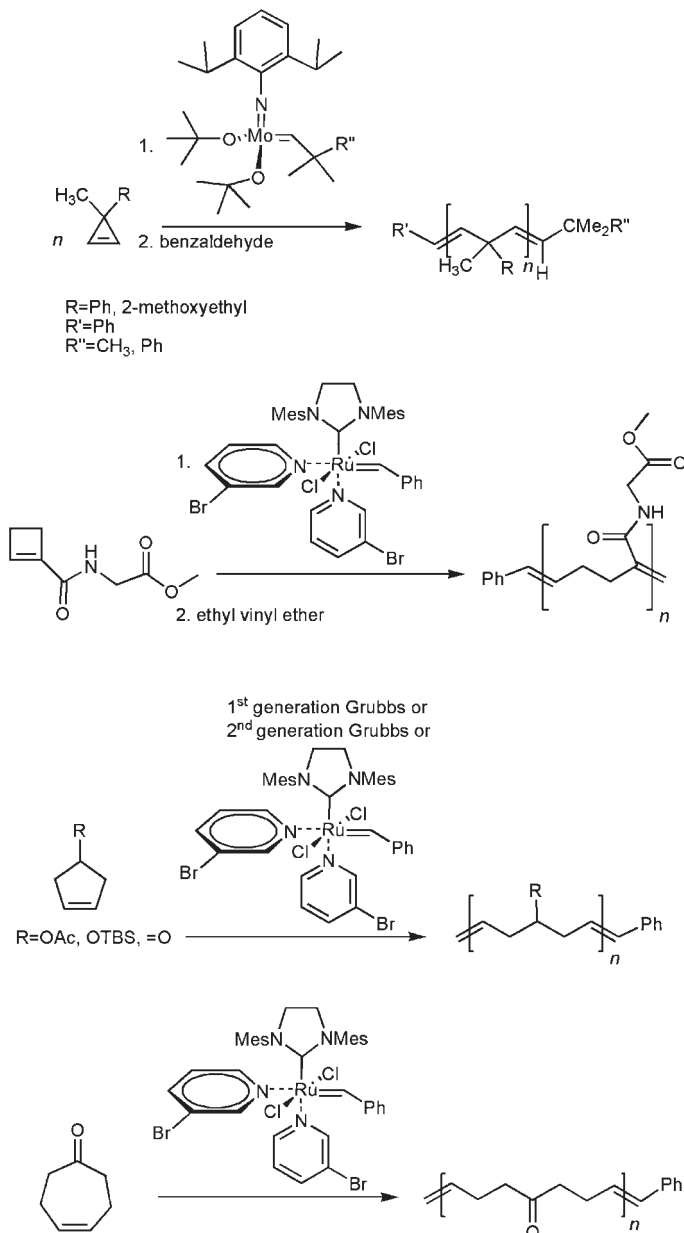
However, perhaps the most striking advance in catalyst design was the development of pyridine-containing second-generation Grubbs-type catalysts (Scheme 8.9) [133]. Thus, the dipyridine derivative of a Grubbs' second-generation catalyst exceeded that of all known phosphane analogues [134] in terms of initiation by a factor 100 to 10^5 , and was only bettered by the corresponding bis(3-bromopyridine) derivative. In particular, the latter is currently probably the best initiating Grubbs-type catalyst for ROMP, as it displays highly favorable ratios of k_i over k_p , allowing for the living polymerization of a series of functional norborn-2-ene derivatives [135].

8.5.2

ROMP of High and Low Ring-Strain Monomers

Recently, Schrock *et al.* extended 'living' ROMP to the polymerization of cyclopropenes (Scheme 8.10) [136]. 3-Methyl-3-R-substituted cyclopropenes ($R = Ph$, 2-methoxyethyl) were polymerized using $Mo(N-2,6-2-Pr_2-C_6H_3)(OC(CH_3)_3)(CHCMe_2Ph)$ and $Mo(N-2,6-2-Pr_2-C_6H_3)(OC(CH_3)_3)(CHCMe_3)$, respectively, to yield polymers with low PDI (<1.05). Sampson *et al.* reported on the polymerization of amino acid-functionalized cyclobutenes using $RuCl_2(3-Br-Py)_2(IMesH_2)(CHPh)$ ($IMesH_2 = 1,3$ -dimesityl-4,5-dihydroimidazolin-2-ylidene) [137]. Thus, a stereoregular, all-*E*-configured poly(cyclobutene) with pendant amino acids was formed (Scheme 8.10). Grubbs *et al.* reported on the polymerization

of low-ring strain cyclic olefins such as (functional) cyclopentenes and cycloheptenes using $\text{RuCl}_2(\text{PCy}_3)_2(\text{CHPh})$, $\text{RuCl}_2(\text{PCy}_3)(\text{IMesH}_2)(\text{CHPh})$ and $\text{RuCl}_2(3\text{-Br-Py})_2(\text{IMesH}_2)(\text{CHPh})$, respectively [138]. Reasonable, but not quantitative polymer yields were obtained, and PDIs were <1.8 throughout (Scheme 8.10).



Scheme 8.10 ROMP of high- and low-ring strain monomers.

8.5.3

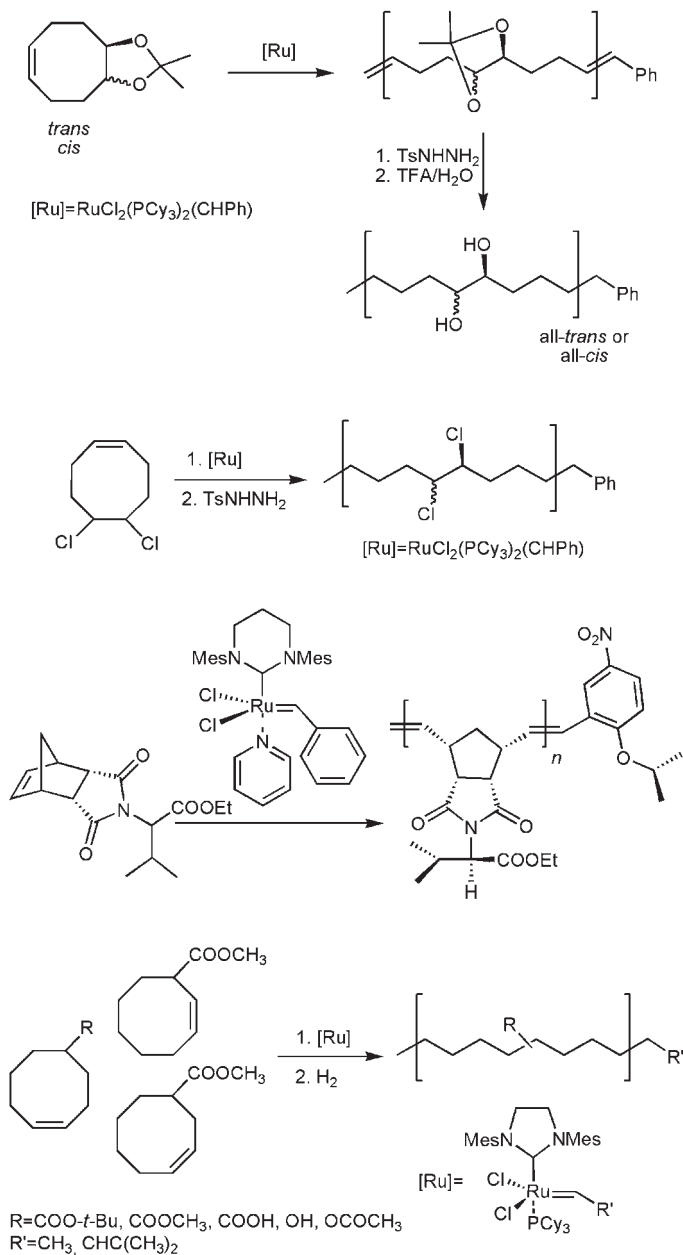
Stereoselective and Regioselective ROMP

Grubbs *et al.* reported on regioregular and stereoregular ethylene–vinyl alcohol copolymers via ROMP of symmetric, *vic*-, acetate-, carbonate- or acetonide-protected cyclooctenediols using both $\text{RuCl}_2(\text{PCy}_3)_2(\text{CHPh})$ and $\text{RuCl}_2(\text{PCy}_3)(\text{IMesH}_2)(\text{CHPh})$ [139]. Well-controlled polymerizations were observed (Scheme 8.11). Hydrogenation and deprotection yielded polymers that may formally be described as ‘alternating’ copolymers, consisting of two consecutive ethylene and two consecutive vinyl alcohol units with the latter two in a head-to-tail connectivity. The relative stereochemistry of the two *vic*-hydroxy groups could be predetermined via the stereochemistry of the parent (protected) cyclooctene monomer. Rowan *et al.* described the polymerization of 5-chlorocyclooctene with $\text{RuCl}_2(\text{PCy}_3)_2(\text{CHPh})$ (Scheme 8.11) [140]. The resultant polymer represents an alternating copolymer of vinyl chloride with 1,3-butadiene. Hydrogenation yields a formal copolymer of vinyl chloride with ethylene. As head-to-tail and head-to-head connectivities occurred simultaneously, the position of the chlorine atoms was not defined in both polymers. Buchmeiser *et al.* reported on the ROMP of enantiomerically pure monomers, *exo*-*N*-(norborn-2-ene-5-carboxyl)-*L*-phenylalanine ethyl ester and *endo*, *endo*-*N,N*-(norborn-5-ene-2,3-dicarbimido)-*L*-valine ethyl ester using $\text{RuCl}_2(\text{Py})(1,3\text{-dimesityl-3,4,5,6-tetrahydropyrimidin-2-ylidene})(\text{CHPh})$ and $\text{RuCl}_2(1,3\text{-dimesityl-3,4,5,6-tetrahydropyrimidin-2-ylidene})(\text{CH-2-(2-PrO-5-NO}_2\text{-C}_6\text{H}_3))$, respectively [141]. An all-*trans* structure was assigned to poly(*endo*, *endo*-*N,N*-(norborn-5-ene-2,3-dicarbimido)-*L*-valine ethyl ester) (Scheme 8.11). Finally, Wagener *et al.* published details of the formal synthesis of poly(ethylene-*co*-vinyl alcohol), poly(ethylene-*co*-vinyl acetate), poly(ethylene-*co*-methylacrylate) and poly(ethylene-*co*-acrylic acid) copolymers, obtained via the ROMP of cyclooctene with hydroxy-, acetoxy-, methoxy-carbonyl and carboxylate-functionalized cyclooctenes, followed by hydrogenation [142]. High-molecular weight polymers with $M_w < 370\,000\text{ g mol}^{-1}$ were obtained using $\text{RuCl}_2(\text{IMesH}_2)(\text{PCy}_3)(\text{CHCH}_3)$ (Scheme 8.11) [130].

8.5.4

Mechanistic Investigations

Kenwright and Koshravi *et al.* performed an appealing study on the ROMP of norborn-2-ene-based monomers with oxygen-containing groups in the 7- or 2-position, using $\text{RuCl}_2(\text{PCy}_3)_2(\text{CHPh})$ and $\text{RuCl}_2(\text{PCy}_3)(\text{CH-2-(2-PrO)-C}_6\text{H}_4)$, respectively [143]. In contrast to pure hydrocarbon-based monomers, where the $\text{RuCl}_2(\text{PCy}_3)_2(\text{CHPh})$ -derived propagating species (not the transition state!) is a bisphosphane coordinated Ru-complex, mono-phosphane–Ru complexes were found in the ROMP of oxygen-containing monomers, initiated by either of the two initiators. Here, the second coordination site is coordinated by the oxygen containing ligand. These findings are in accordance with results reported by Grell *et al.* [144], who described Grubbs–Hoveyda-type initiators with additional carbonyl groups on the benzyldiene ligand. In case these were in vicinity to the Ru-moiety, an additional coordination of these carbonyl groups to the Ru was observed, thus



Scheme 8.11 Stereoselective and regioselective ROMP.

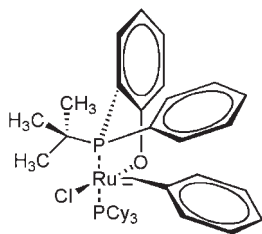


Figure 8.6 P,O-dichelating first-generation Grubbs-type initiator for alternating ROMP of norborn-2-ene and cyclooctene.

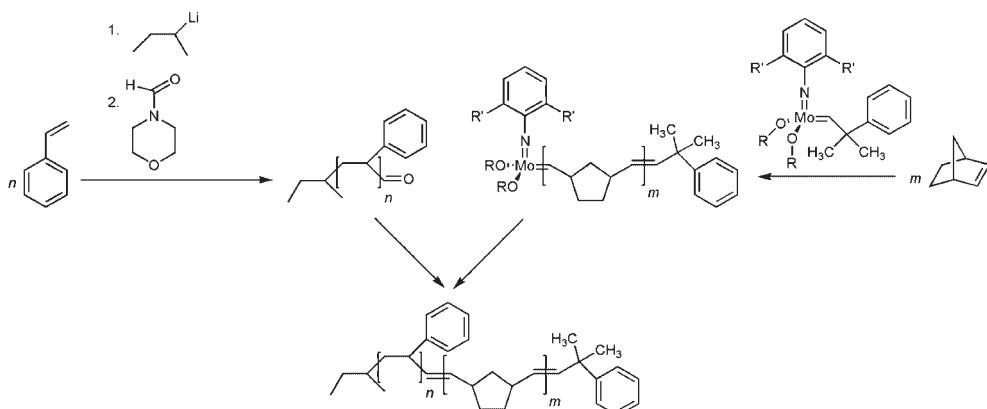
illustrating the high proneness of the metal to bind to oxygen-containing ligands. Interestingly enough, the polymerization of 7-*t*-butoxybicyclo [2.2.1]hepta-2,5-diene with $\text{RuCl}_2(\text{CHPh})(\text{PCy}_3)_2$ did *not* lead to the desired polymer, but rather to cyclic products and regeneration of the initiator. So far, this exclusive cyclization reaction has only been observed for this particular monomer [145]. When Koshravi *et al.* reinvestigated this process, however, they could not identify a valid mechanistic explanation for these findings [146]. In terms of instrumental analysis, Reed *et al.* reported on the use of automatic, continuous on-line monitoring of polymerization (ACOMP) reactions [147]. This chromatographic technique entails the continuous withdrawal of a small sample stream from a polymerization. Subsequent dilution and analysis of the single particle properties by multi-angle light scattering (MALS), UV absorption, viscometry or differential refractometry allowed the determination of both reaction kinetics and mechanisms.

8.5.5

Alternating Copolymerizations

Very few reports have been made on the alternating copolymerization of different monomers via ROMP [148–151]. More recently, the alternating copolymerization of cyclooctene with a norborn-5-ene-2,3-dicarboximide derivative was described by Coughlin *et al.* [152]. Using a P,O-dichelating first-generation Grubbs-type initiator (Figure 8.6), Chen *et al.* observed—along with other pure poly(norborn-2-ene) and poly(cyclooctene) sequences—the alternating incorporation of norborn-2-enen and cyclooctene in the copolymerization of these two monomers [153].

Bergens *et al.* reported on the construction of a catalyst-containing organic framework produced by the alternating ROMP of cyclooctene and a bis (norborn-5-ene-2,3-dicarboximide)-based monomer with a bridging, chiral 2,2'-diphosphane-binaphthyl ligand [154]. The immobilization of a Ru(II) catalyst allowed for the production of a reusable chiral catalyst for ketone hydrogenation. Rooney *et al.* reported on the alternating copolymerization of norborn-2-ene and cyclopentene using $\text{RuCl}_2(\text{PCy}_3)_2(\text{CHPh})$, $\text{RuCl}_2(\text{P}(2\text{-Pr})_3)_2(\text{CHSPh})$ and $\text{RuCl}_2(\text{P}(2\text{-Pr})_3)(\text{CHCH}_2(2\text{-pyridyl}))$ in the presence of Lewis acids such as MoCl_5 and WCl_6 . A 'cage effect' served as an explanation for the restricted access of the (more reactive) norborn-2-ene [151]. Interestingly, $\text{RuCl}_2(\text{IMesH}_2)(\text{PCy}_3)(\text{CHPh})$ did *not* give rise to alternating copolymerizations, whether in the absence or presence of Lewis acids.



Scheme 8.12 Coupling of 'living' anionic polymerization to 'living' ROMP.

8.5.6

Changes in Polymerization Mechanism

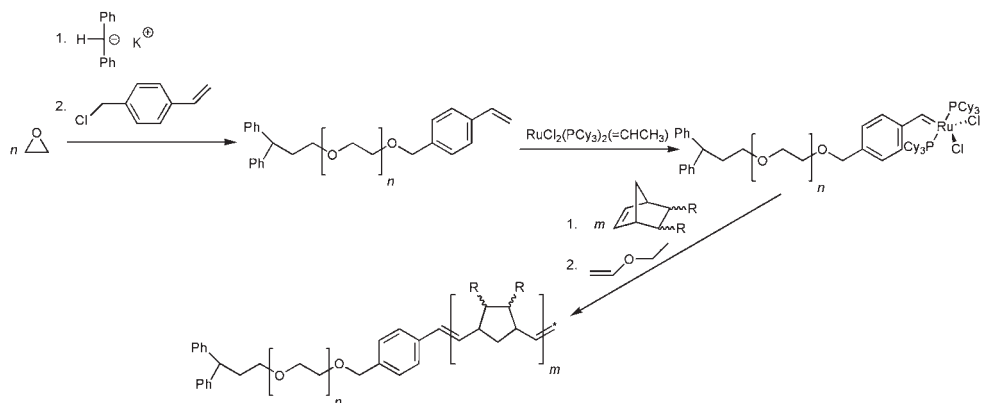
Hillmyer *et al.* reported on the synthesis of a bis(dodecyltrithiocarbonate) functionalized *cis*-but-2-ene-1,4-diol and its use as chain-transfer agent in the ROMP of cyclooctene, applying $\text{RuCl}_2(\text{PCy}_3)(\text{IMesH}_2)(\text{CHPh})$ [155, 156]. The ditelechelic polymer was then used in radical addition–fragmentation–transfer (RAFT) polymerization. By using this approach, poly(butadiene-*b*-cyclooctene-*b*-butadiene) tercopolymers with PDIs < 1.3 were realized. The coupling of living anionic polymerization to ROMP was first described by Feast *et al.* [157], while Register *et al.* coupled 'living' anionic polymerization-derived poly(styrene) and poly(isoprene), respectively, to ROMP-derived living poly(norborn-2-ene) and poly(cyclopentene), respectively (Scheme 8.12) [158]. For this purpose, the 'living' anionic polymerization was terminated with N -formylmorpholine to yield aldehyde-terminated polymers that were then reacted with a Schrock catalyst-terminated, 'living' ROMP-derived polymer. In this Wittig-type reaction, both polymer chains were coupled together, yielding low-PDI diblock copolymers.

Recently, Khosravi reported on the change in polymerization mechanism from 'living' anionic polymerization to ROMP. For this purpose, poly(ethylene oxide) (PEO) was polymerized with $\text{Ph}_2\text{CH}^-\text{K}^+$ and terminated with 4-chloromethylstyrene. The thus-obtained vinyl-terminated PEO was then reacted with $\text{RuCl}_2(\text{PCy}_3)_2(\text{CHPh})$ and used for the ROMP of 2,3-difunctional norborn-2-enes to yield the desired poly(PEO-*b*-NBE) block copolymer (Scheme 8.13) [159].

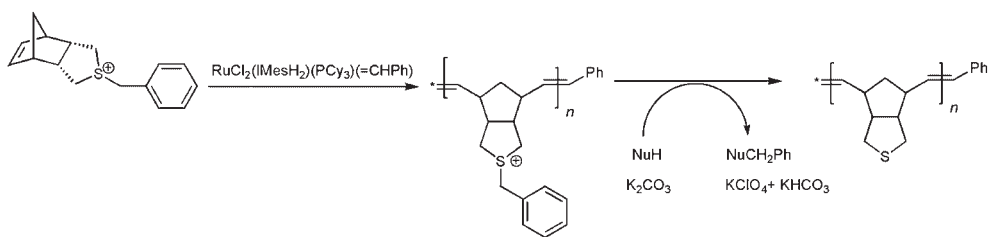
8.5.7

Materials Science

Bis(norborn-2-ene) functionalized hexabenzocoronene was allowed to self-assemble into a kinetic intermediate—that is, a coiled assembly—as well as into thermodynamically stable nanotubes. ROMP of the surface-attached norborn-2-enes into



Scheme 8.13 Coupling of 'living' anionic polymerization to ROMP.



Scheme 8.14 Polymer-supported benzylsulfonium perchlorates.

poly(norborn-2-enes) using $\text{RuCl}_2(\text{PCy}_3)(\text{MesH}_2)(\text{CHPh})$ allowed for the 'freezing' of both structures, and thus represents a very nice approach to the stabilization of intermediary, three-dimensional structures [160]. ROMP was first used for the synthesis of crosslinked, surface-functionalized particles by our group [24, 161–164], and these materials were subsequently used for applications in the areas of separation science and heterogeneous catalysis. In addition, the synthesis of ROMP-derived (functional) particles and lattices has been described by others [165–172]. For example, Barrett *et al.* used the concept of precipitation polymerization [24, 161–164] to construct functional ROMP-derived particles for use in parallel synthesis [173]. More recently, these materials have been used for the immobilization of *seco*-porphyrazines and as photo-oxygenation catalysts [174], as well as for the synthesis of 1-alkynes from aldehydes using a supported 1-diazo-2-oxopropylphosphonate reagent [175]. Flynn and Hanson *et al.* reported on the synthesis of norborn-2-ene-tagged benzylsulfonium perchlorates, whereupon ROMP by the action of $\text{RuCl}_2(\text{IMesH}_2)(\text{PCy}_3)(\text{CHPh})$ yielded an insoluble oligomer (Scheme 8.14) [176].

The thus-obtained supported reagent was used for the benzylation of various amines and phenols. Recently, Janda *et al.* reported on a suspension-type ROMP of mixtures of norborn-2-ene, hydroxymethylnorborn-2-ene and a norborn-2-ene-derived crosslinker for the synthesis of hydroxyl-functionalized spherical supports [177]. After hydrogenation, the support was successfully used for

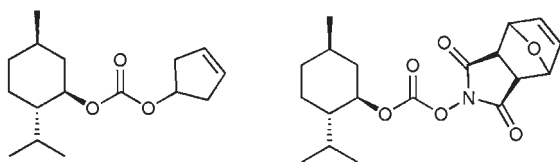


Figure 8.7 Chiral monomers used for molecular imprinting.

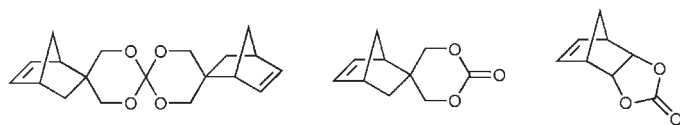


Figure 8.8 Norborn-2-ene-based, cyclic carbonate-containing monomers.

various solid-phase synthetic applications. Schubert *et al.* reported on the synthesis of an organic/inorganic interpenetrating network obtained via ROM copolymerization of a norborn-2-ene-substituted Ti-oxo-propoxide cluster with norborn-2-ene, using $\text{RuCl}_2(\text{PCy}_3)_2(\text{CHPh})$ [178]. A random distribution of the Ti-cluster within the organic framework was confirmed by X-ray scattering. Steinke *et al.* used ROMP for the synthesis of molecularly imprinted polymers (MIPs). Here, enantiomerically pure menthyl-cyclopent-4-ylcarbonate as well as *exo, exo*-*N*-(*L*-menthyloxycarbonyl)-7-oxanorborn-5-ene-2,3-dicarboximide (Figure 8.7) were copolymerized with norborn-2-ene and dicyclopentadiene, respectively [179, 180]. When the first-generation Grubbs' catalyst $\text{RuCl}_2(\text{PCy}_3)_2(\text{CHPh})$ was used for polymer synthesis, mixtures of D- and L-menthol could be enriched on the MIP up to 10% enantiomeric excess (ee).

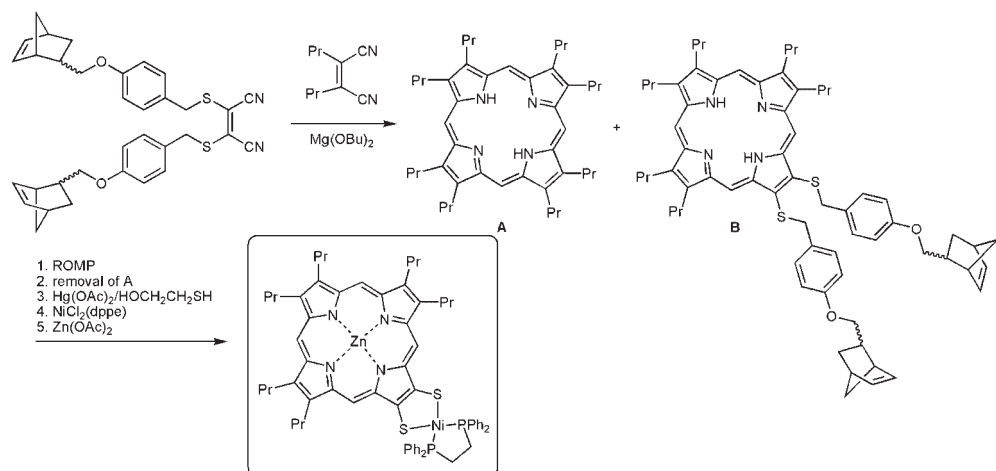
Endo *et al.* reported on the ROMP of norborn-2-enes with pendant or annelated five- and six-membered cyclic carbonates [181]; the monomers are shown in Figure 8.8. Surprisingly, the monomers showed a *volume increase* during ROMP, rendering them highly interesting candidates for tooth implants. Jérôme *et al.* described the ROMP of unsaturated ϵ -caprolactone, 6,7-dihydro-2(3*H*)-oxepinone, using $\text{Mo}(\text{N}-2,6\text{-Me}_2\text{-C}_6\text{H}_3)(\text{OCMe}(\text{CF}_3)_2)(\text{CHCMe}_2\text{Ph})$ [182] to yield an unsaturated ROMP-derived polyester with molecular weights in the range of 20 000 to 60 000 g mol^{-1} . Barrett *et al.* reported on a ROMP capture-release approach for the synthesis of porphyrazine derivatives (Scheme 8.15) [183, 184].

8.5.8

ROMP in Water and in Ionic Liquids

ROMP in water was first described by the group of R.H. Grubbs [1, 44], although more recent systems have entailed the use of poly(ethylene glycol)-substituted pyridines for initiator synthesis (Figure 8.9) [185].

Although the final catalyst displayed ROMP activity in water versus *N*-triethyleneglycol-substituted 7-oxanorborn-5-ene-2,3-dicarboximide, the polymerization was found to be pH-sensitive and to proceed without the usual control over



Scheme 8.15 ROMP capture–release approach to the synthesis of porphyrazine derivatives.

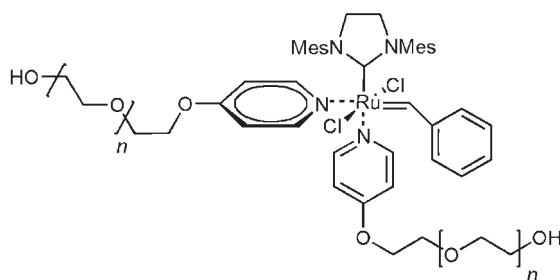


Figure 8.9 4-Poly(ethylene glycol)-substituted pyridine-derived Grubbs-type initiators.

molecular weight and PDI. Buchmeiser *et al.* reported on the first ROMP of various functional norborn-2-enes in pure ionic liquids (ILs) in the absence of any organic solvent [186]. As a consequence, the ILs were found to be an attractive alternative to polymerizations in standard organic solvents, and notably so for those monomers that are insoluble in the latter. The ILs also allowed for recycling of the catalyst. Unfortunately, however, both the cation and anion of the IL had to be selected carefully in order to avoid interaction with the catalyst, as well as exchange of the anion [187].

8.5.9

Computational Studies

Fomine and Tlenkopatchev *et al.* reported on computational studies on the use of 1,2-difluoroethylene as a chain-transfer agent in the ROMP of norborn-2-ene initiated by $\text{RuCl}_2(\text{PCy}_3)_2(\text{IMesH}_2)(\text{CHPh})$ [155]. These calculations revealed a remarkable stability of the resulting ruthenium fluoromethylidene species

$\text{RuCl}_2(=\text{CF}_2)(\text{IMesH}_2)$, thus explaining the comparable low activity of fluorine substitutes alkenes in metathesis reactions.

8.6

Summary and Prospects

Developments in the area of initiators for ROMP have resulted in the creation of a large armory of transition-metal compounds suited to these purposes. In addition, while the mechanistic details of Schrock-type initiators are well established, the mechanistic understanding of ROMP—particularly with ruthenium-based initiators—has experienced impressive progress such that today, highly sophisticated polymeric architectures can be produced that quite recently were barely achievable with other polymerization methods. Yet, further progress in both polymer and materials science may well be expected.

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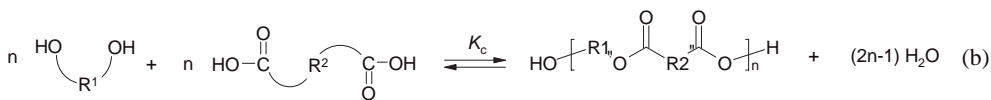
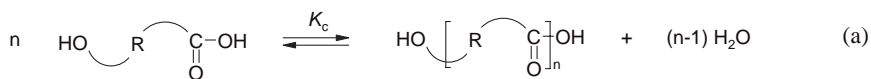
9

Polyesters from β -Lactones*Olivier Coulembier and Philippe Dubois***9.1****Introduction**

Polyesters, defined as heterochain macromolecules containing repeating ester groups in the main chain, were historically first synthesized via step-growth polycondensation. This ‘polyesterification’ is based either on the homo polycondensation of hydroxycarboxylic acid (Scheme 9.1a) or the hetero polycondensation of a diol with dicarboxylic acid (Scheme 9.1b), where R, R¹ and R² denote alkylene groups. Unfortunately, in order to reach high-molar-mass polymers based on these processes, a sufficiently high equilibrium constant (K_c) is required and, in the case of heteropolycondensation, a 1:1 stoichiometry must be strictly obeyed. Alternatively, the ring-opening polymerization (ROP) of lactones and related cyclic monomers has currently become a more simple and attractive method for the preparation of such aliphatic main-chain polyester. This allows the synthesis and preparation of ‘tailor-made’ polymers which exhibit a high molecular weight, a unimodal molecular weight distribution, and other useful properties that often are requested in medicinal and pharmacological applications. The traditional chemistry of lactone ROP has been well reviewed [1] but, with regards to the multiple studies conducted to date, many factors may influence the course of lactone polymerization, including:

- the size of the monomer ring
- the position, number and nature of the substituents on the ring
- the reaction parameters, such as the type of initiator, catalyst, solvent, monomer concentration and temperature
- unfortunate possible side reactions based on transesterification; these include back-biting and/or end-to-end biting, and chain transfer to foreign macromolecules followed by chain rupture.

For all of these reasons, the chemistry of lactones polymerization is considered not only very complex but also delicate. Moreover, as has been reviewed by others,



Scheme 9.1 Polyesterification based on either
(a) homopolycondensation and (b) heteropolycondensation.

when many different species are active during a polymerization process, attempts to identify general rules valid for all lactones and similarities in the mechanisms of vinyl monomer polymerization, have failed.

In this chapter we review the basic principles of polyester synthesis produced from 2-oxetanone-type monomers (named β -lactones), including details of pertinent mechanistic aspects and the general properties of the resultant polymeric materials. Before discussing the ROP of β -lactones, however, we provide a brief overview of the synthesis of β -lactone key derivatives.

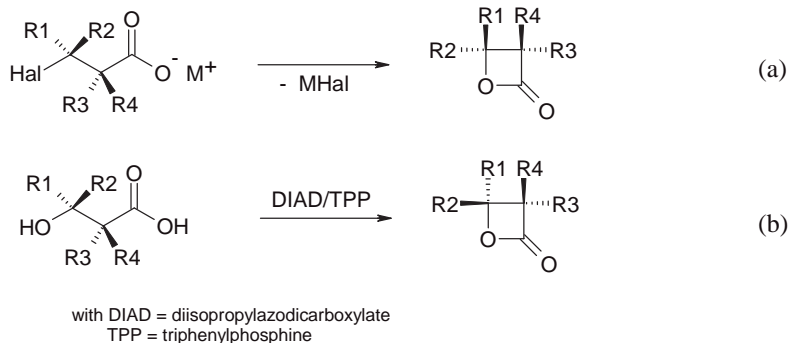
9.2

β -Lactones Preparation

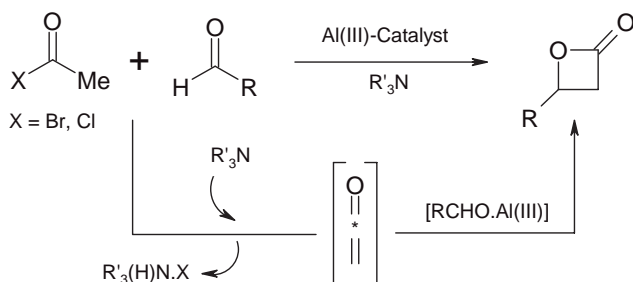
Interest in β -lactones has increased greatly during the past 30 years with the recognition that these heterocycle systems constitute the key structural feature in a number of biologically interesting natural products [2]. Such interest has emerged due to use of the strained 2-oxetanone ring as an important versatile synthetic intermediate. As a representative example, their intrinsic reactivities have been exploited in the synthesis of propionic acid [3], tetrahydrofurans [4] and α -amino acid derivatives [5], as their nucleophilic cleavage takes place under relatively mild conditions with a variety of (non)organometallic reagents and heteroatom nucleophiles.

Since the first representative of this class of heterocycles was prepared in 1883 [6], the synthetic routes for β -lactones have much attention. The synthetic procedures generally involved the cyclization of β -halocarboxylate salts [7] (the Knoevenagel reaction) (Scheme 9.2a) and the diazotation of β -amino acids [8]. Moreover, under Mitsunobu conditions, β -hydroxy acids undergo a similar cyclization (Scheme 9.2b) [5, 9]. Although these methods have been successfully and widely employed, it should be noted that their use is often limited by side reactions, including β -elimination and decarboxylative elimination. This problem is due to the inherent instability/fragility as well as the high boiling points of certain β -lactones. Nonetheless, in 1996 Guérin *et al.* were able to demonstrate the positive effect of multistep purifications in order to obtain highly pure β -lactones, in reproducible yields [10].

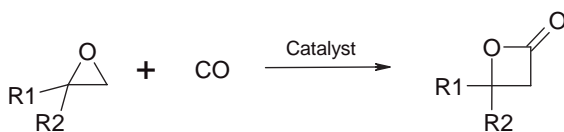
The direct conversion of ketones and aldehydes to β -lactones in a single step has been successfully realized. For example, as ketenes have been shown to



Scheme 9.2 Synthesis of β -lactone from (a) β -halocarboxylate salts and (b) β -hydroxy acids.



Scheme 9.3 Synthesis of β -lactones from aldehydes.



Scheme 9.4 Synthesis of β -lactones from epoxides.

participate in a Lewis acid-catalyzed [2+2] cycloaddition with carbonyl compounds [4, 7], β -lactones can result from an addition reaction involving ynonate anions [11] or via catalyzed acyl halide-aldehyde cyclocondensation (AAC) reactions (Scheme 9.3) [12].

Interestingly, β -lactone monomers can also be obtained by the carbonylation of epoxides using metal complexes, as recently reinvestigated by Coates *et al.*, who developed discrete cationic Lewis-acid complexes of $\text{Co}(\text{CO})_4^+$ which exhibited unprecedented activities for epoxide carbonylation and provided access to the corresponding β -(di)substituted β -lactones (Scheme 9.4) [13, 14].

In the following sections, the polymerization of β -lactones will be discussed with regards to the nature of the active species, whether anionic, cationic, coordination-type or carbene-based. Finally, a brief overview will be provided of the enzymatic ROP of four-membered lactones.

9.3

Ionic Polymerization

9.3.1

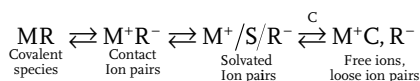
Anionic Processes

Anionic polymerization has an essential role in the polyester synthesis from lactones because it enables the correct design of the polymer's molecular weight, structure and properties. As has been widely reviewed, the anionic ROP of four-membered lactone monomers takes place by the nucleophilic attack of a negatively charged initiator on the carbonyl carbon, or on the carbon atom adjacent to the endocyclic ether oxygen atom, resulting in linear polyester (Scheme 9.5).

As already highlighted, depending on:

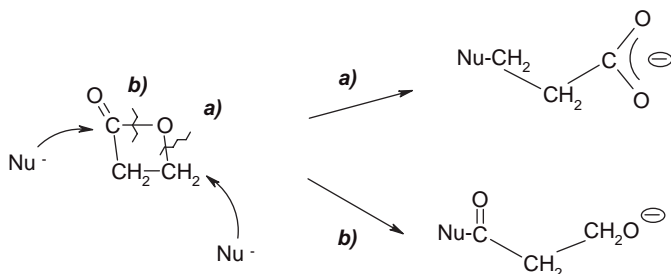
- the nature of the ionic propagating chain end (alkoholate, carboxylate, or both simultaneously),
- the solvent polarity,
- the nature and size of the associated counterion and,
- the presence (or not) of a complexing cation agent

the reactive growing end-group can vary from completely ionic (free ions) to almost covalent species:



where S is the solvent and C is a complexing cation agent, for example, a crown ether or a cryptand.

Associated with this well-known propagating species equilibrium, β -lactones behave differently to other larger lactones, due to their high polarity and high internal strain of the four-membered ring (Table 9.1). Since 1948, when details of the β -propiolactone (PL) ionic polymerization were first published [20], much more information regarding the polymerization not only of β -lactones but also of substituted β -lactones, has become available [21–27].



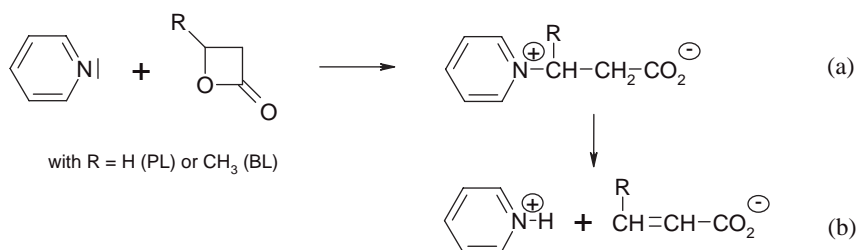
Scheme 9.5 ROP of four-membered cyclic ester monomers by either (a) alkyl-oxygen or (b) acyl-oxygen bond cleavage (illustration with β -propiolactone).

Table 9.1 Standard thermodynamic parameters of polymerization for selected lactones (298 K)

Parameter	Monomer				
	PL	γ -BL	VL	LA	CL
Ring size	4	5	6	6	7
Conditions ^a	lc	lc	lc	ss	lc
ΔH_p (kJ mol ⁻¹)	-82.3	5.1	-27.4	-22.9	-28.8
ΔS_p (J mol ⁻¹)	-74	-29.9	-65.0	-25.0	-53.9
$[M]_{eq}$ (mol l ⁻¹)	2.8×10^{-11}	2.9×10^2	3.9×10^{-2}	1.0×10^{-3}	6.0×10^{-3}
Reference	[15]	[16]	[17]	[18]	[19]

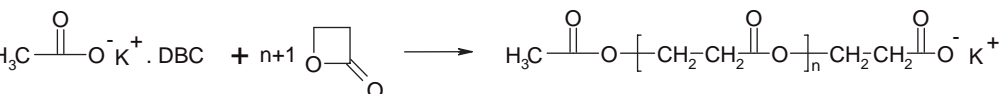
a The first letter denotes the state of monomer, the second that of polymer: l = liquid; c = condensed; s = solution.

PL, β -propiolactone; γ -BL, γ -butyrolactone; LA, L,L-lactide; CL, ϵ -caprolactone.

**Scheme 9.6** Suspected elimination reaction from betain as obtained from β -lactones and amine moieties.

Initially, β -lactone polymerization with organic bases, such as phosphines, pyridines and tertiary amines, was studied in solvents of different polarity [28]. It was first suggested that the initiation step involved the formation of a betain species, followed by a propagation which proceeded via alkyl-oxygen bond cleavage, resulting from the attack of a carboxylate anion on the β -carbon atom of the incoming monomer molecules [28c]. As this suggestion was inconsistent with the respective nucleophilicity-to-basicity ratio of the engaged initiators, it was quickly replaced with an alternative mechanism that proposed a nucleophilic attack to the β -carbon of lactone; the subsequent betain formation (Scheme 9.6a) led to a reaction involving elimination of the protonated base (Scheme 9.6b). This interpretation was well accepted, since the presence of a positive charge close to the β -carbon increased the acidity of the α -protons, thus favoring a deprotonation reaction by a weak base. This assumption, supported by the fact that betains were only obtained from the reaction of lactones with pyridine, but never from triethylamine [28a], highlighted the inability of sterically hindered bases (such as triethylamine) to react with PL, according to Scheme 9.6.

Such deprotonation/elimination side reactions yield either acrylate (from β -propiolactone) or crotonate species (β -butyrolactone) that are also capable of



Scheme 9.7 General scheme for the ‘living’ polymerization of β -propiolactone as initiated by complexed carboxylate salts.
DBC = dibenzo-18-crown-6 ether.

serving as initiating sites, and this leads to functional polymers with unsaturated end-groups. Hence, these reactions proved to be a limiting factor in the control over molecular weight and molecular weight distribution.

When weak bases or ammonium carboxylates are used as initiators, a similar mechanism has been observed which involves the carboxylate anions responsible for propagation. Subsequently, it was confirmed that, in the case of α,α' -dialkyl- β -propiolactone, no chain transfer could occur as α -proton abstraction could no longer take place [29]. Interestingly, a similar result was recently highlighted by Guérin *et al.* who showed that, compared to poly(malolactonate) (as obtained from α,α',β -trisubstituted β -lactones), polymers prepared by the ROP of β -lactones without substitution in the α -position were characterized by major discrepancies between the experimental molecular weights and the theoretical values expected for a controlled/‘living’ polymerization (see below) [30].

In order to avoid the multiple deprotonation observed during β -lactone polymerizations, in 1976 both Boileau and Penczek showed, independently, that the introduction of macrocyclic ligand such as a crown ether [31] or a cryptand [32] in the anionic polymerization of PL (initiated with potassium acetate) would lead to a ‘living’ polymerization (Scheme 9.7). As shown later by same authors, the M_n of the growing polyester became a linear function of monomer conversion, while the semilogarithmic monomer conversion kinetic plot was a linear function of time [33].

The ‘living’ character of the anionic polymerization of PL has enabled determination of the absolute rate constants of propagation on free macroions ($k_p^{(-)}$) and macroion pairs ($k_p^{(\pm)}$), since the overall propagation rate coefficient was shown to be the result of various forms of active species. For the polymerization of PL in CH_2Cl_2 or in dimethylformamide (DMF), the reactivity of the macroion pairs was found to be almost independent of the initial monomer concentration, and weakly dependent on the temperature [33a,b] (cf. ΔH_p^\ddagger in Table 9.2).

As emphasized by these authors, an inversion temperature (T_i):

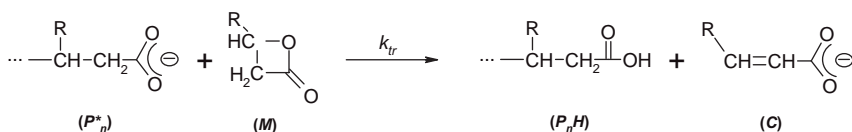
$$T_i = (\Delta H_p^\ddagger(-) - \Delta H_p^\ddagger(\pm)) / (\Delta S_p^\ddagger(-) - \Delta S_p^\ddagger(\pm)) \quad (9.1)$$

then exists when $\Delta H_p^\ddagger(-) > \Delta H_p^\ddagger(\pm)$. Such an interpretation leads to the fact that the free ions are more reactive than ion pairs above T_i , whereas below this temperature the free ions are the less-reactive species. For the polymerization of PL, the T_i -values were calculated as being equal to -35°C in CH_2Cl_2 ($[M]_0 = 3 \text{ mol l}^{-1}$) [33a], and to 20°C in DMF ($[M]_0 = 1 \text{ mol l}^{-1}$) [33b]. In comparison, in the polymerization of substituted β -lactone such as α -methyl- α -propyl- β -propiolactone,

Table 9.2 Thermodynamic parameters for the polymerization of β -propiolactone in CH_2Cl_2 or DMF [33].

$[\text{M}]_0$ (mol l^{-1})	Solvent	$\Delta H_p^\#(-)$ (kJ mol^{-1})	$\Delta H_p^\#(\pm)$ (kJ mol^{-1})	$\Delta S_p^\#(-)$ ($\text{kJ mol}^{-1} \text{ K}^{-1}$)	$\Delta S_p^\#(\pm)$ ($\text{kJ mol}^{-1} \text{ K}^{-1}$)
0.0	CH_2Cl_2	25 ± 4	25 ± 4	-167 ± 21	-218 ± 17
3.0	CH_2Cl_2	67 ± 1	25 ± 4	-42 ± 17	-218 ± 17
0.5	DMF	88 ± 9	52 ± 8	34 ± 6	95 ± 4
1.0	DMF	114 ± 9	61 ± 9	105 ± 9	64 ± 6

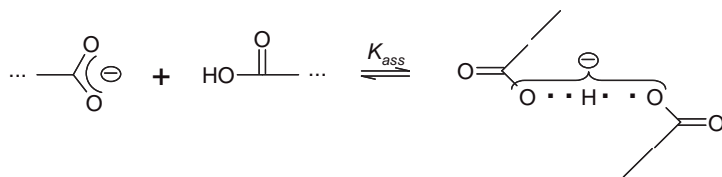
DMF = dimethylformamide.

**Scheme 9.8** Transfer reaction to β -substituted β -lactone monomer from carboxylate active sites.

Haggiage *et al.* showed the macroion pairs to be more reactive than macroions in THF, at low temperature [33c].

Interestingly—and in contrast to the unsubstituted, four-membered β -propiolactone— β -butyrolactone is not polymerized by common anionic initiators such as metal alkoxides and alkali metal carboxylate salts [34]. However, these initiators, when activated by the addition of macrocyclic ligands such as crown ethers, are able to initiate the polymerization of β -butyrolactone. Recent results have also highlighted the possible oligomerization of β -butyrolactone when initiated by (*R,S*)-3-hydroxybutyric acid in a highly polar aprotic solvent such as dimethyl sulfoxide (DMSO) [35]. On the basis of more detailed studies, it was later shown that at room temperature there was already a measurable transfer to monomer (Scheme 9.8) [36]. The propagation-to-transfer rate constant ratios were determined as equal to $k_p/k_{tr} = 4.0 \times 10^4$ for PL (CH_2Cl_2 solvent, 20°C), and $k_p/k_{tr} \leq 2.0 \times 10^2$ for β -butyrolactone (BL) (THF solvent, 20°C). Both electronic and steric effects of the methyl substituent were assumed to be responsible for a lower value of the k_p/k_{tr} ratio in BL when compared to PL (see Scheme 9.8), where *M* denotes the monomer (PL if *R* = H; BL if *R* = CH_3), P_n^* is the active propagating center, P_nH are the macromolecules of poly(*M*) with an acidic chain-end, *C* is the acrylate or crotonate species, and k_{tr} is the rate constant of transfer.

By taking into account these reactions, and preventing the progress of the ROP for ‘living’ and controlled polymerizations (especially in the case of BL), two kinetic effects have been established [36]. The first effect results from a reinitiation with the crotonate anions, and leads to a reduction in the polymer molecular weight: the M_n -values of the resultant poly(*M*) are, at the start of polymerization, close to those calculated from Equation 9.2:



Scheme 9.9 General scheme of the carboxylate anions complexation with carboxylic acid moieties.

$$M_n = ([M]_0 - [M]) \times M_w(M) / ([I]_0 + [H]_{tot} - [C]_{tot}) \quad (9.2)$$

where $M_w(M)$ is the molecular weight of monomer M , $[I]_0$ is the initial initiator concentration, $[H]_{tot}$ the total concentration of protons (both in carboxylic acid and their associates) and $[C]_{tot}$ is the total concentration of crotonate species (associated, protonated, nonassociated and deprotonated forms).

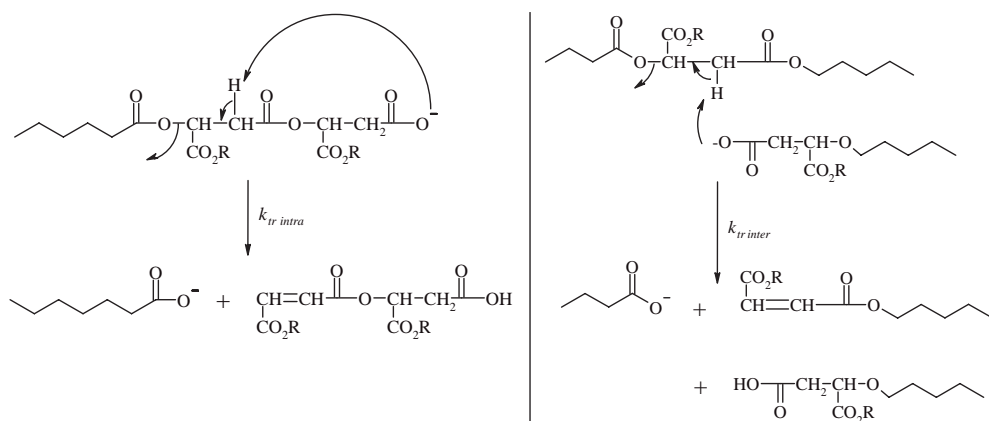
The second effect relies on the decrease in the overall polymerization rate due to complexation of the growing carboxylate anions with carboxylic acid moieties (Scheme 9.9).

Globally, the overall kinetic scheme of BL polymerization involves propagation accompanied by transfer/deprotonation, followed by slow reinitiation reactions.

Assuming that such transfer reactions are associated with the kinetic constants, the limit of M_n for poly(PL) is of the order of 10^6 , whereas for poly(BL) it would be $\sim 1.7 \times 10^4$. However, Jedlinski and coworkers have also demonstrated the possibility of reaching a higher 'predicted' molar mass for the anionic polymerization of butyrolactone [37]. In their studies, carboxylic acid salts were used as initiators, but were complexed by bulky tetrabutyl ammonium (TBA) counterions, thereby allowing the creation of high-molecular-weight polyesters [degree of polymerization (DP) ≤ 2000 and ≤ 360 for the racemic and optically active monomers, respectively]. The remarkable efficiency of TBA was explained by the strong activation effect of this bulky alkylammonium cation on the carboxylate active center, generating much weaker electrostatic interactions with respect to those existing within the normally used sodium carboxylate ion pairs.

Recently it was shown that, in addition to the aforementioned monomer transfer occurring in the initiation step, further undesirable transfer reactions between carboxylate active species and growing polymer chains may also take place along the anionic propagation step of four-membered lactones, such as benzyl- β -malolactonate, as initiated by potassium 11-hydroxydodecanoate complexed by 18-crown-6 ether (Scheme 9.10) [27c]. The reduction of both reaction temperature and monomer concentration led to significant decreases in the extent of transfer and termination reactions (at both the initiation/propagation steps) by proton abstraction. The M_n of the growing polyesters became a linear function of monomer conversion, while the semilogarithmic kinetic plot proved to be a linear function of time (Figure 9.1).

Important progress was also observed in the anionic polymerization of β -lactones initiated by strong bases such as alkali metal alcoholates. As described



Scheme 9.10 Transfer reactions between carboxylate active species and growing poly(β -lactone) chains.

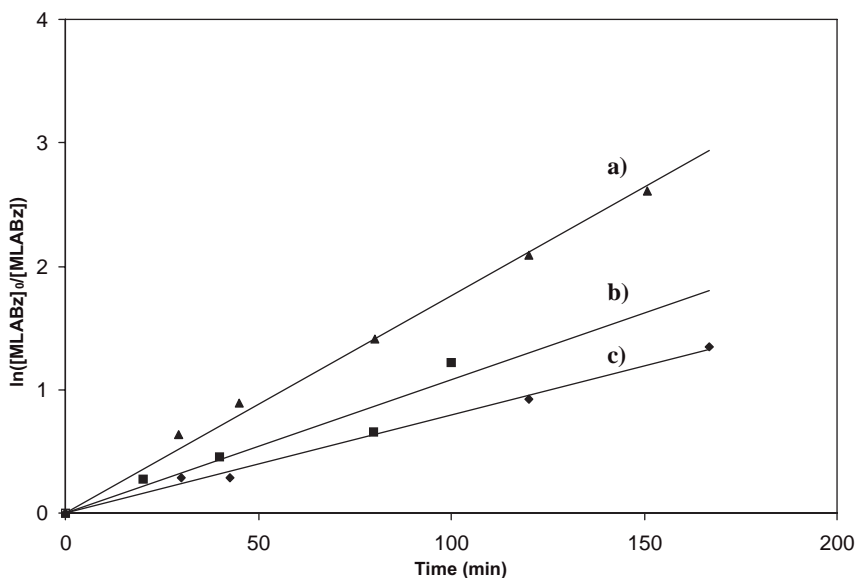
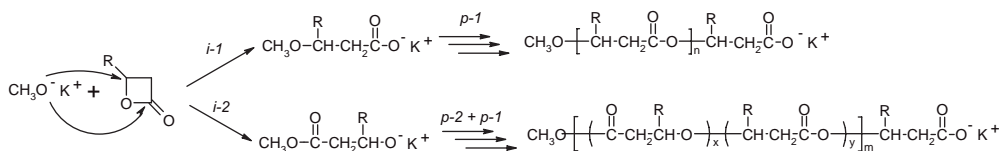
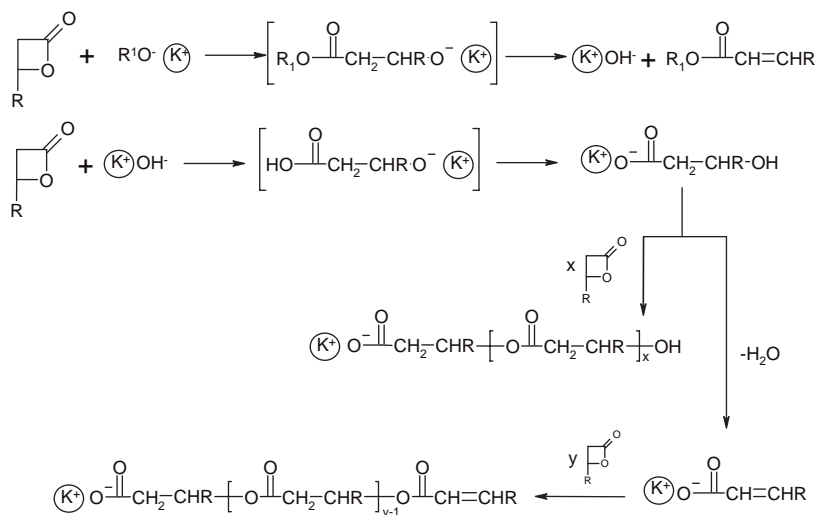


Figure 9.1 Time-dependence of benzyl- β -malolactonate (MLABz) conversion in polyester as initiated by potassium 11-hydroxydodecanoate added with 18-crown-6 ether (HDD) in THF at 0°C for $[\text{MLABz}]_0$ of 0.2 mol l^{-1} and various $[\text{MLABz}]_0/[\text{HDD}]_0$ ratios: (a) 24, (b) 48, (c) 73.

by Penczek *et al.* [38], it was claimed that the initiation and propagation of β -lactone polymerization in DMF with a potassium methoxide initiator proceeded via both alkyl-oxygen and acyl-oxygen bond cleavages, the former being prevalent at the propagation step. The resulting polymers were reported to contain either ether or ester end-groups, due to incorporation of the methoxide initiator at the initiation step (Scheme 9.11).



Scheme 9.11 Model reaction between potassium methoxide and β -lactones, where i-1 and i-2 denote the initiation process after alkyl-oxygen and acyl-oxygen cleavages, respectively; p-1 and p-2, propagation steps from carboxylate and alcoholate active centers, respectively). (Adapted from Ref. [36].)



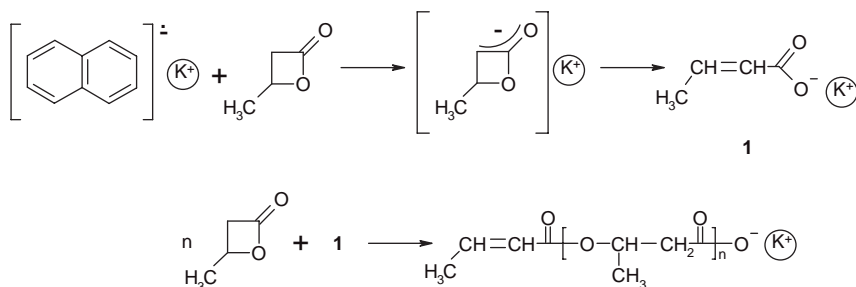
where $\text{R} = \text{H}$ or CH_3 ; $\text{R}_1 = \text{CH}_3$ or $\text{C}(\text{CH}_3)_3$

$\text{K}^+ = (\text{K}^+, 18\text{-crown-6})$ complex

Scheme 9.12 Model reaction between potassium methoxide and β -lactones. (Adapted from Refs [39–42].)

Later, Dale—followed by Kricheldorf—observed the presence of carbon–carbon double bonds at the extremities of polymers formed in the so-performed polymerization of β -lactones [39, 40]. According to experimental results [41, 42], the initiation involved a nucleophilic attack at the carbonyl carbon atom of a monomer by the alkoxide anion of the initiator, cleaving the acyl–oxygen bond to yield the corresponding potassium alkoxide of the respective β -hydroxycarboxylic acid esters (Scheme 9.12). The acidic α -proton abstraction involved the formation of an unsaturated ester due to KOH elimination. Finally, polymerization occurred in the case involving β -lactone in excess, with the KOH acting as initiator.

Since alkali metal naphthalenides have been claimed not to polymerize β -lactones at room temperature [43], the polymerization of β -lactones from those

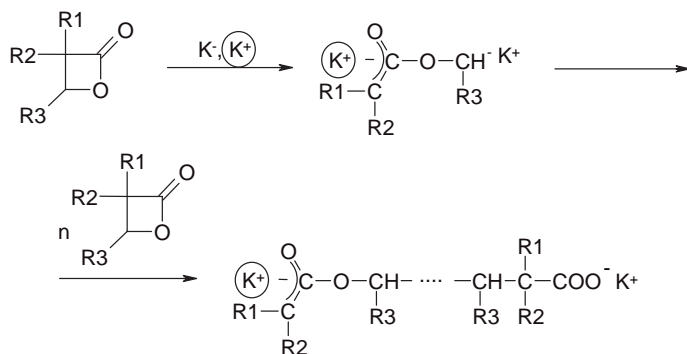


Scheme 9.13 Ring-opening mechanism of β -butyrolactone using complexed alkali metal naphthalenide [44].

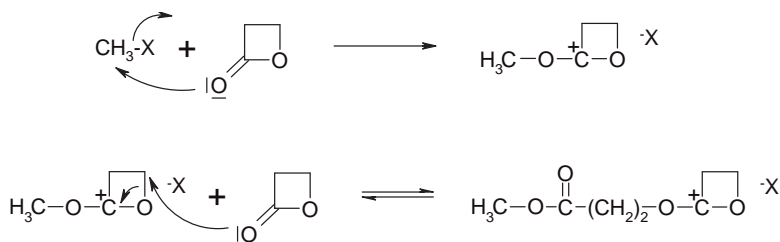
initiators has been somewhat ‘forgotten’ for more than 25 years. Interestingly, however, after the addition of a crown ether (which is capable of potassium cation complexation) this system proved to be highly efficient, yielding functionalized polyesters that exhibited carbon–carbon bonds at one end-group. The polymerization mechanism proposed by Jedlinski and coworkers is shown in summary form in Scheme 9.13 [44].

Supramolecular metal complexes such as $K^+/15\text{-C-}5/K^-$; $K^+/18\text{-C-}6/K^-$; $K^+/\text{glyme}/K^-$; and $K^+/15\text{-C-}5/Na^+$, where $18\text{-C-}6 = 18\text{-crown-}6$, $15\text{-C-}5 = 15\text{-crown-}5$ and $\text{glyme} = \text{CH}_3\text{-O-(CH}_2\text{)}_2\text{-O-CH}_3$, can be prepared in a simple manner by the dissolution of solid metal (potassium mirror or sodium–potassium alloy) in an organic solvent containing organic ligands. Indeed, such purpose-built complexes—with defined concentrations of metal ions—have been widely prepared and used as potential initiators for the polymerization of four-membered lactones. Of course, the nature of the active centers and the propagation mechanism of the polymerization of β -PL with such initiators was first studied, with Jedlinski and colleagues noting that model reactions between β -lactone monomer and the potassium anion revealed a single electron transfer from the metal anion to the β -lactone molecule. This resulted in the formation of a lactone radical anion, as proven by electron spin resonance (ESR) measurements and ^{39}K -NMR [45]. The proposed mechanism of ring opening involved an uncommon α -carbon to β -carbon bond scission, with the formation of an enolate carbanion capable of opening a cyclic monomer [46, 47]. As expected, under normal polymerization conditions, when the monomer is available in excess, the enolate carbanion initially formed attacks the monomer to produce growing polymer chains.

The nature of the active centers formed at various stages of the polymerization has also been elucidated in several model experiments. The authors concluded that the propagation would proceed on alkoxide and carboxylate active centers, respectively formed by the acyl–oxygen and alkyl–oxygen bond scissions of the monomer. The number of carboxylate active sites was also found to increase with the DP, such that they became prevalent on completion of the reaction (Scheme 9.14) [48].



Scheme 9.14 Ring-opening mechanism of β -lactone using complexed alkali metal [48].

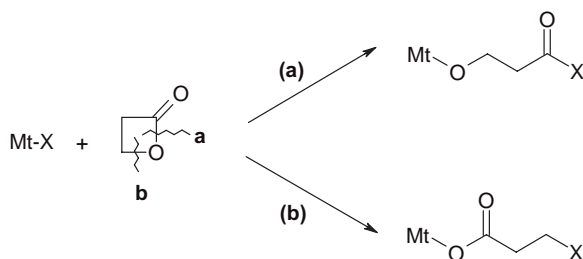


Scheme 9.15 Cationic ring-opening polymerization mechanism of β -lactone from alkylating initiator.

9.3.2

Carbocationic Process

As noted by several authors, due to the occurrence of intramolecular transesterification, proton and hydride transfer reactions, carbocationic ROP is less useful than anionic polymerization for obtaining high-molecular-weight polyesters. The cationic polymerization of β -lactones has been studied using a variety of cationic promoters, including protic acids (HCl , RCOOH , RSO_3H , etc.), Lewis acids (AlCl_3 , BF_3 , FeCl_3 , ZnCl_2 , etc.), alkylating agents (e.g. stable carbenium salts or oxonium salts such as $\text{Et}_3\text{O}^+\text{BF}_4^-$) and acylating agents (e.g. acylium ions). Despite much effort, the cationic polymerization of β -lactones is not yet sufficiently well understood, as the nature of the active sites has not been fully identified for all of the studied reactions. However, independently of the nature of the initiator applied, the cationic polymerization initiated by alkylating or acylating initiators is generally believed to proceed via alkyl-oxygen bond cleavage of the monomer, with the initiator being incorporated into the growing polymer chains (Scheme 9.15) [49]. Today, this mechanism is commonly accepted, having been attested by the determination of end-group structure by cation trapping using triphenyl phosphine [49d].



Scheme 9.16 ‘O-acyl’ (a) and ‘O-alkyl’ (b) cleavages of β -lactone monomer.

9.4

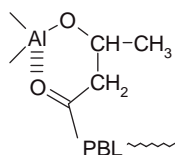
Coordination Process

Depending on the nature of both monomer and catalyst, the ROP of four-membered lactones can also proceed according to two mechanistic pathways which involve either a C(O)–O bond ‘acyl’ cleavage to form a metal alkoxide growing species (Scheme 9.16a), or by C $_{\beta}$ –O bond ‘alkyl’ cleavage leading to metal carboxylate growing species (Scheme 9.16b).

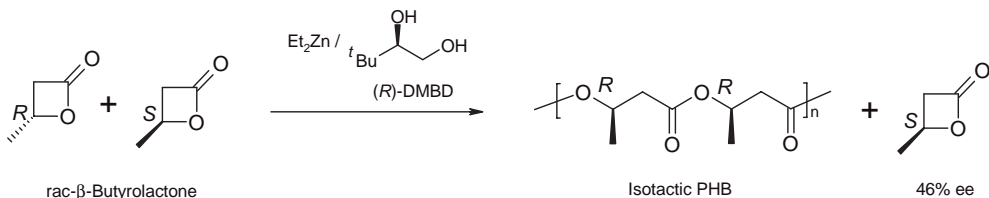
Among the multinuclear and mononuclear active species evaluated for lactone polymerization, those effective for the polymerization of β -lactones implying an ‘O-acyl’ scission (Scheme 9.16a) are aluminum and dialkylaluminum alkoxides, yttrium alkoxides, zinc alkoxides, aluminoxanes, zincoxanes, bimetallic μ -oxoalkoxides and aluminum porphyrins of the (TPP)AlOR type [50]. However, aluminum porphyrins such as (TPP)AlCl or (TPP)AlOC(O)R and aluminum Schiff’s base complexes such as (Sal)AlCl (where Sal = salenato group) are able to promote lactone polymerization by ‘O-alkyl’ scission (Scheme 9.16b) [50].

Although Sn(II) 2-ethylhexanoate [Sn(Oct) $_2$] was proposed as one of the most frequently used catalysts for the polymerization of lactones and lactides, the mechanism involved has been the subject of much controversy with regards to the type of ring cleavage involved [51]. By comparison, the aluminoxane-catalyzed polymerizations of β -substituted β -lactones present certain drawbacks, including a long polymerization time, broad sample polydispersity, and the formation of a product mixture of isotactic and atactic polymers of various molecular weights when polymerization is carried out from racemic mixture (*R,S*) of β -lactones; this was demonstrated by Lenz and coworkers for the polymerization of β -monosubstituted β -propiolactones, using trialkyl aluminum–water catalysis [52]. However, these shortcomings may be eradicated by using a bulkier catalyst such as isobutylaluminoxane to achieve a higher-molecular-weight poly(BL) [53].

The (*R,S*)-BL polymerization by aluminum alkoxides [aluminum triisopropoxide, Al(O i Pr) $_3$] proceeds via a coordination–insertion mechanism [54]. At low monomer-to-initiator molar ratios, an atactic polyester is formed, although syndiotacticity predominates when the initiator is added with nicotine. The authors suggested that the slow rate of polymerization was due to intramolecular coordination of the Al atom with the carbonyl group of the penultimate unit, thus reducing the



Scheme 9.17 Intramolecular coordination of Al atom with penultimate carbonyl group in ROP of BL, as initiated by $\text{Al}(\text{O}^i\text{Pr})_3$ [54].



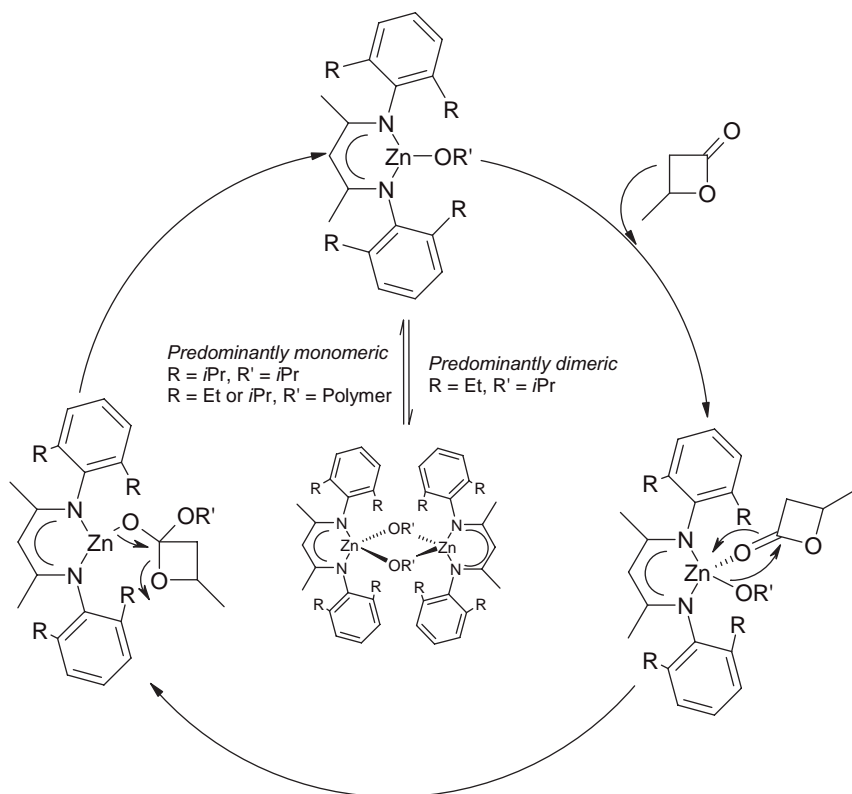
Scheme 9.18 Isospecific polymerization of racemic-BL [56].

activity of the alkoxide and making monomer insertion more difficult (Scheme 9.17). At a higher monomer-to-initiator ratio (ca. 170), there is competition between the propagation and the (inter- and intra-molecular) transesterification (and elimination) reactions, such that control over the poly(BL) molecular weight is lost (as indicated by the appearance of crotonate species in the reaction medium).

In 1994, a highly efficient yttrium-based catalyst–yttrium 2-methoxyethoxide–was applied successfully to the polymerization of BL, with the reaction proceeding readily at room temperature [55]. When compared to diethylzinc/water or diethylzinc/methanol catalytic systems, the enantioasymmetric polymerization of racemic BL was also carried out in the presence of a diethylzinc/(*R*)-(–)-3,3-dimethyl-1,2-butanediol catalytic system (Scheme 9.18) [56].

Varying the substitution of the β -lactone, by using racemic α -ethyl- α -methyl- β -propiolactone or α -propyl- α -methyl- β -propiolactone, led to the production of an optically active polymer which obeyed stereoselection in the presence of a diethylzinc/(*R*)-(–)-3,3-dimethyl-1,2-butanediol catalytic system, whereas the diethylzinc/methanol system led only to atactic polymers [56–58]. These findings indicated that the enantiomorphic sites of the zinc coordination catalyst were unable to recognize the chirality of the lactone monomer used for the polymerization. It should also be noted here that an antisteric type of stereoselection in the polymerization of racemic α -propyl- α -methyl- β -propiolactone was reported when dimethylcadmium/(*R*)-(–)-3,3-dimethyl-1,2-butanediol was used as catalyst [56].

In a recent report, Coates *et al.* showed that (*R*)-diiminate zinc alkoxide complexes could polymerize *rac*-BL very rapidly under mild conditions, and in a controlled manner [59]. Consistent with a ‘living’ process, high-molecular-weight materials were obtained at room temperature, and with a fairly narrow polydispersity. However, all of the polyesters produced were all atactic and obtained by insertion of the BL monomer into the alkoxide chain-end, mediated by the monometallic zinc complex (Scheme 9.19). Ring-opening was seen to occur via acyl-oxygen bond cleavage, such that the configuration at the chiral methine carbon was retained. However, several results also suggested that the elimination side

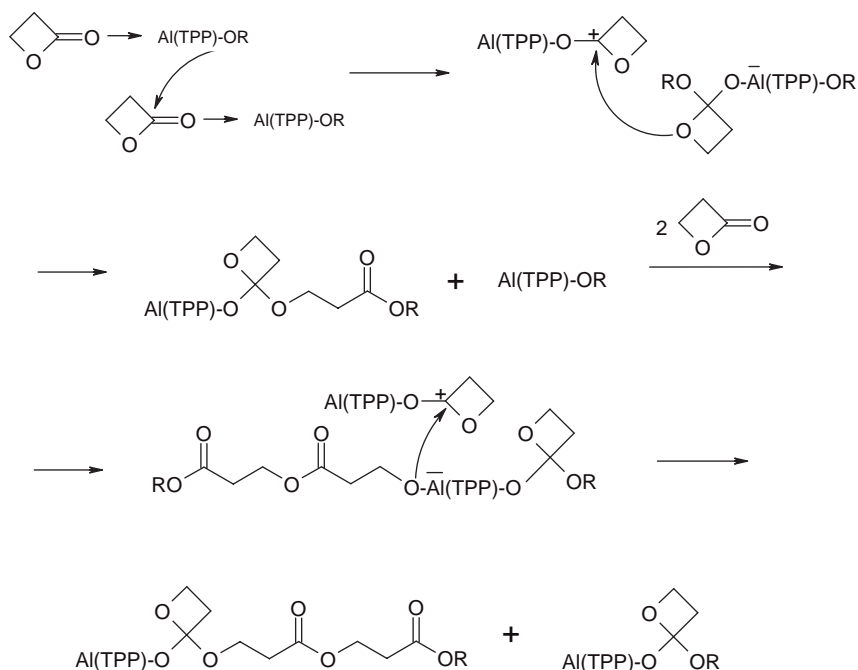


Scheme 9.19 Proposed mechanism for the ROP of BL by (R)-diiminate zinc alkoxide catalyst. (Adapted from Ref. [59]).

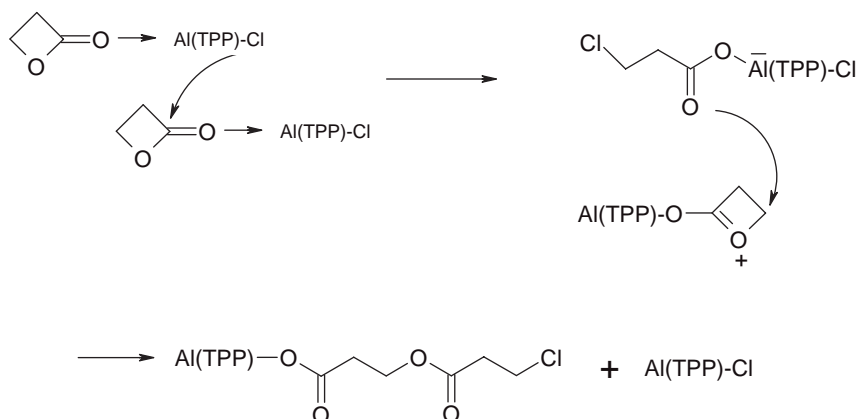
reactions were also slowly catalyzed by zinc alkoxides, leading to some loss of molecular parameter control.

In the case of lactone polymerization with the (TPP)AlOR catalyst, ring-opening via C(O)–O bond cleavage involves the participation of two catalyst molecules; these can be presented schematically for the polymerization of β -lactone, as in Scheme 9.20 [60, 61]. The polymerization of BL in the presence of (TPP)AlCl, (TPP)AlOC(O)R or (Sal)AlCl catalysts, which involves cleavage of the C _{β} –O bond, can be explained in terms of the nucleophilic attack being carried out with the participation of another catalyst molecule for coordinating the monomer (Scheme 9.21) [62–65].

Importantly, it has been shown that a Lewis acid with bulky substituents, such as methylaluminum di(2,6-di-*t*-butyl-4-methylphenoxy), exhibits an accelerating effect on the polymerization of β -lactones, with the extent of acceleration depending on the mode of lactone ring cleavage. The polymerization of BL in the presence of (TPP)AlOMe (Scheme 9.20) was slower than the ROP conducted with (TPP)AlCl (Scheme 9.21), but the accelerating effect of the bulky Lewis acid was more significant for the (TPP)AlOMe catalyst [63]. Thus, such acceleration is considered to

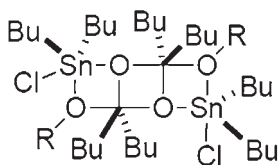


Scheme 9.20 Proposed mechanism for the ROP of β -lactone by TPP aluminum alkoxide [60].



Scheme 9.21 Proposed mechanism for the ROP of β -lactone by TPP aluminum chloride [62].

be due to a coordination of the carbonyl oxygen atom of the lactone at the aluminum atom of the Lewis acid. Such coordination was seen to affect the reactivity directly when the carbonyl group was attacked by the growing species, whereas the attack at the C_β atom, which is remote from the carbonyl group, was less affected by the coordination and resulted in different extents of acceleration, depending on the mode of ring cleavage.



Scheme 9.22 Distannoxane initiator.

R = OMe, OEt

The first demonstration of the synthesis of predominantly syndiotactic PBL starting from *rac*-BL with tin-based initiators was reported in 1993 [66]. It was shown that a polymerization carried out at 40°C with Bu_3SnOMe gave a low-molecular-weight PBL that was enriched by syndiotactic dyads of 0.7 (probability of syndiotactic dyads $P_r = 0.70$). By comparison, other catalytic systems (e.g. alkyltin methoxides and oxides) which had been reported to catalyze the syndiospecific polymerization of *rac*-BL [67] were very modest, and the associated polymerizations were characterized by a low-molecular-weight poly(BL). Recently, however, distannoxane catalysts (Scheme 9.22) were shown by Hori [68] and Giani-Beaune [69] to afford predominantly syndiotactic PBL ($P_r = 0.67$) by a chain-end control mechanism and characterized by their high molecular weight.

Despite recent significant advances in the ROP of cyclic esters, the number of selective and productive initiators remains modest. Interestingly enough, Group III metal complexes supported by amino-bis(phenolate) ligands have been recently reported as efficient initiators in the ROP of BL [70]. Such initiators exhibit a very high polymerization activity and productivity, combined in some cases with high stereoselectivity and effective chain transfer to alcohol additives. The high selectivity for the chain-end controlled polymerization of *rac*-BL was achieved by employing steric hindrance on the aromatic rings.

9.5

Carbene-Based Polymerization

N-heterocyclic carbenes (NHCs) are by far the most well-studied members of the family of nucleophilic carbenes [71]. Although they are generally known as excellent ligands for metal-based catalysis, they are attracting increasing interest as organocatalysts. Metal-free catalyzed processes represent interesting alternatives to classical organic transformations as they are often more economical and environmentally friendly. The high reactivity of NHCs for transesterification reactions is also highlighted by their ability to catalyze the ROP of lactones. In 2002, the 1,3-bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene (IMes) carbene was shown to catalyze the ROP of BL to generate poly(β -butyrolactone) (PBL) of defined molecular weight and narrow polydispersity, but with a low DP-value of 50 [72]. Since this first report, extensive studies have been conducted to exploit the wide structural and electronic diversity of NHCs for the ROP of different monomers [73–75]; however, very few of these studies have been directly involved with investigations into the ROP of β -lactones.

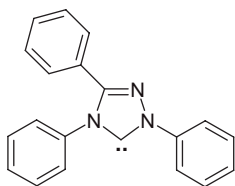


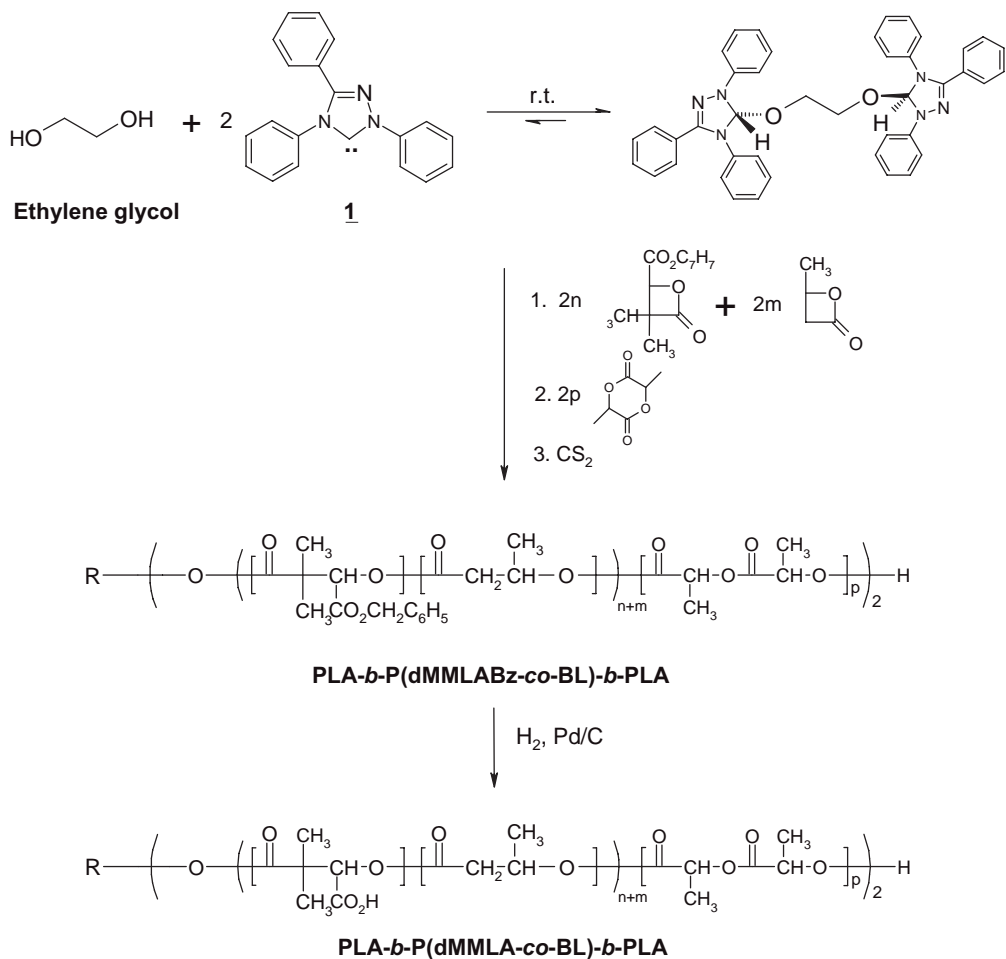
Figure 9.2 Molecular structure of commercially available 1,3,4-triphenyl-4,5-dihydro-1H-1,2-triazol-5-ylidene.

The selectivity of the commercially available 1,3,4-triphenyl-4,5-dihydro-1H-1,2-triazol-5-ylidene carbene **1** (Figure 9.2) for the ROP of lactide prompted Coulemier and coworkers to investigate its reactivity in the ROP of BL [76]. The group showed that, when the polymerization of BL was initiated from primary alcohol and **1** at 80°C in toluene, the expected polymer chains were contaminated with crotonate byproducts.

In reasoning that *tert*-butanol could not initiate the polymerization of BL- (although it does react reversibly with the triazole to form the corresponding adduct), the basicity of free **1** and its relative concentration were lowered by the addition of a tertiary alcohol cosolvent to favor adduct formation. Under these conditions, PBL polymers were obtained with molecular weights that matched those predicted from the monomer-to-initiator ratios and narrow polydispersities (for molecular weights with DP < 200). For such low DP-values, the plot of molecular weight versus conversion for **1**-catalyzed ROP proved linear, and was more likely consistent with a ‘living’ polymerization in which the monomer cleavage proceeded by an O–acyl scission.

Based on these results, the same group proceeded to synthesize polylactide-*block*-(dimethyl β -malic acid-*co*- β -butyrolactone)-*block*-polylactide (PLA-*b*-P(dMMLA-*co*-BL)-*b*-PLA) triblock copolymers, according to a totally original three-step strategy [77]. In a first step, the ROP of dimethyl benzyl β -malolactonate (dMMLABz) and BL was carried out in toluene/*t*-BuOH solvent mixture at 80°C by using ethylene glycol as initiator and carbene **1** as catalyst. The ROP mechanism selectively involved the O–acyl cleavage of both dMMLABz and BL cyclic comonomers, with a preferential incorporation of dMMLABz units in the growing polyester chains, as attested by ¹H-NMR spectroscopy. In a second step, the so-produced α,ω -dihydroxy P(dMMLABz-*co*-BL) copolyesters were further considered as a difunctional macroinitiator in a L,L-lactide (LA) monomer ROP at 90°C. In the third and last step, the benzylic ester functions pending along the so-recovered PLA-*b*-P(dMMLABz-*co*-BL)-*b*-PLA triblock copolymers were reduced/deprotected by catalytic hydrogenation, leading to the expected PLA-*b*-P(dMMLA-*co*-BL)-*b*-PLA symmetric and amphiphilic triblock copolyesters (Scheme 9.23).

These combined data demonstrated end-group fidelity and predictable molecular weights, particularly for targeted DP-values of 200 or less. However, BL polymerization targeting higher molecular weights (DP 250–450), generally accompanied by long reaction times, tended to show some broadening in the molecular weight distribution. Moreover, for these high molecular weights a detectable amount of crotonate was observed (up to ~25% of total chain ends), consistent with a second mode of polymerization [76].



where R : $-(\text{CH}_2)_2-$

Scheme 9.23 Three-step strategy route for the synthesis of amphiphilic PLA-*b*-P(dMMLA-co-BL)-*b*-PLA triblock copolymers (where R = $-\text{CH}_2-\text{CH}_2-$) [77].

In 2007, Coulembier *et al.* emphasized the importance of polymerizing BL in anhydrous *t*-BuOH as being the only solvent capable of eliminating even negligible amounts of the undesirable crotonate species that would initiate subsequent propagations and lead to loose molecular weight and end-group fidelities, especially for high-DP targets [78]. Under such conditions, molecular weights in excess of $30\,000\text{ g mol}^{-1}$ were obtained from an equimolar mixture of primary alcohol and **1** at 80°C . Interestingly, an end-group analysis of the polyester chains revealed the presence of carboxylic acid end-groups, which suggested that the carboxylates were the actual propagating species in this polymerization reaction, which was carried out

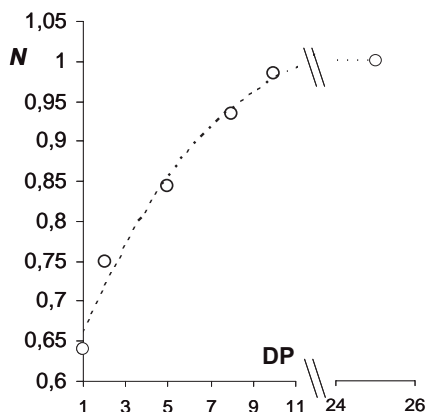
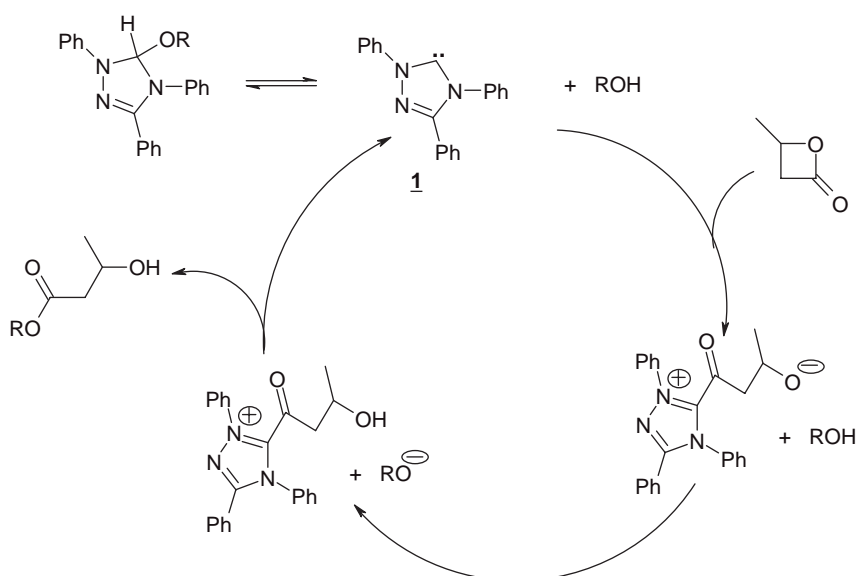


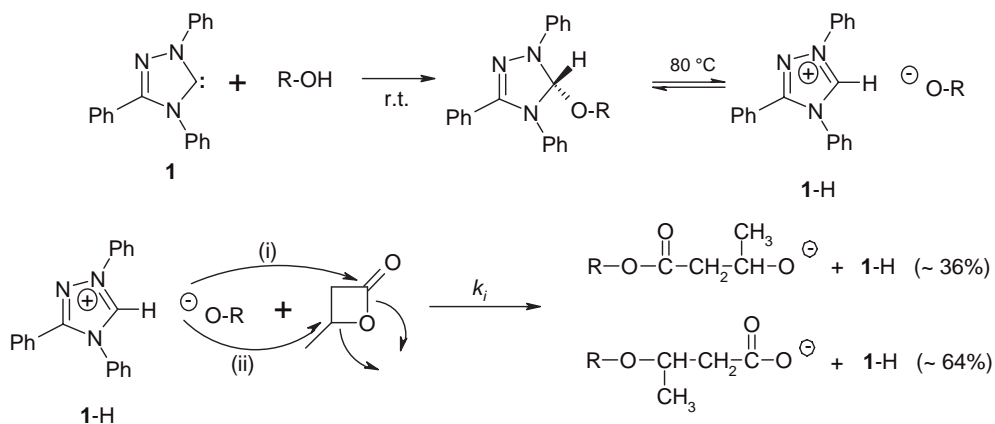
Figure 9.3 Relationship between the average number of growing carboxylate end-groups per PBL oligomer with respect to the alkoxy end-groups (N) and the correlated DP [78].



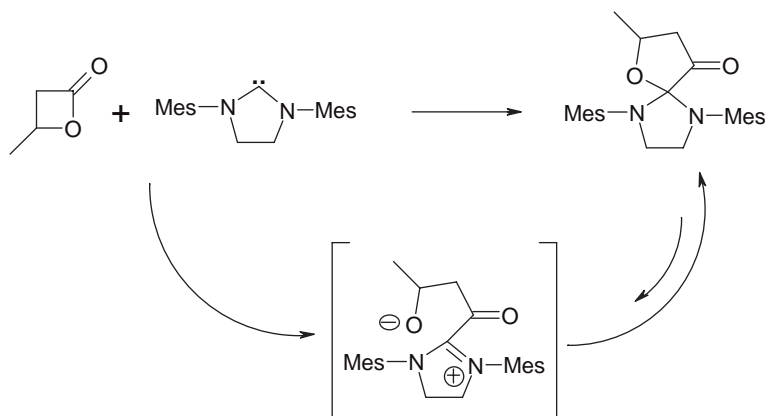
Scheme 9.24 ROP of BL when initiated from an equimolar mixture of primary alcohol and **1** in toluene/ t -BuOH mixture.

exclusively in t -BuOH. The authors showed that both alkoxy and carboxylate groups were present at the early stage of the reaction, while the average number of carboxylate end-groups per polymer chain increased during the course of polymerization, finally to represent the only propagating center for DPs > 10 (Figure 9.3).

Interestingly, it is worth noting that such results allowed the initiation of polymerization from an equimolar mixture of carboxylic acid and **1** at 80 °C in t -BuOH, also to gain access to high-molecular-weight PBL ($M_n > 30\,000\text{ g mol}^{-1}$) [78]. To summarize, even if the NHC-catalyzed ROP proceeds via a suspected monomer-activated mechanism in a toluene/ t -BuOH mixture (Scheme 9.24) [76], clear-cut evidence for an anionic mechanism has been highlighted when polymerization is



Scheme 9.25 Proposed anionic process of BL ROP using alkoxytriazolium adduct as initiator in *t*-BuOH at 80 °C, implying both 'O-acyl' (i) and 'O-alkyl' (ii) cleavages (k_i = initiating rate constant).



Scheme 9.26 Formation of spirocycles from BL and saturated carbenes.

conducted in *t*-BuOH as the only solvent [78]. In such a process, the carbene **1** is suspected to deprotonate the primary alcohol just before the initiation step to produce the corresponding alkoxide, counterbalanced by the protonated **1** as the complexing cation (Scheme 9.25). The resultant alkoxide might then initiate the BL ROP by both O-acyl and O-alkyl scission, while the number of carboxylate end groups per polymer chain increased during the course of polymerization.

Interestingly, the treatment of 1,3-dimesitylimidazolin-2-ylidene NHC (SIMes) with 1 equiv. of BL generated the corresponding spirocycle (Scheme 9.26) [79]. In such a reaction, a zwitterion is generated by a nucleophilic attack of the carbene on BL, followed by neutralization of the opposite charges and leading to the formation of a spirocycle that proved to be a competent initiator for the BL ROP [79]. Remarkably, no linear precursor is involved in any step of the synthesis, and

macrocyclic polyesters are produced accordingly at high monomer concentrations (low dilution).

9.6

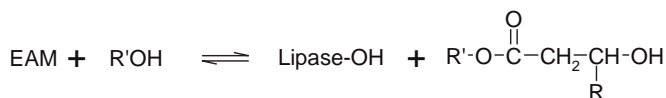
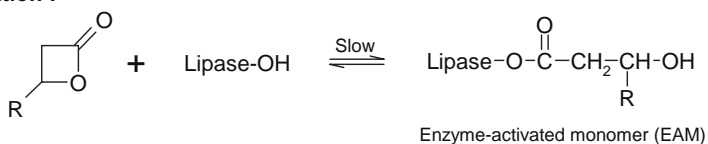
Enzymatic Polymerization

To date, many investigations have been conducted on the (non)-substituted four-membered lactone polymerizations using enzymes as catalysts. The rate-determining step in the overall polymerization scheme corresponds to the formation of the enzyme-activated monomer (EAM), which itself is obtained by reaction of the monomer with the catalytic site of the lipase (serine residue), followed by ring-opening cleavage [80].

Even when alcohol and amine are present at the start of the polymerization reaction, the initiation step has been shown to proceed initially by a nucleophilic attack of a water molecule onto the acyl carbon of the intermediate to produce ω -hydroxy carboxylic acid species. This is then followed by an esterification of the carboxylic acid end-group when the nucleophile is engaged as initiator. In the propagation step, a nucleophilic attack of the terminal hydroxyl group of the ω -hydroxy ester on the EAM leads to the formation of a new chain-extended alcohol (Scheme 9.27).

In the enzyme-catalyzed synthesis of aliphatic, unsaturated and semi-aromatic polyesters from diesters and diols in organic solvents, macrocyclic rings are formed concurrently with the linear chains, with a relative proportion heavily dependent on both the monomer structure and the initial concentration of all reactive groups [81].

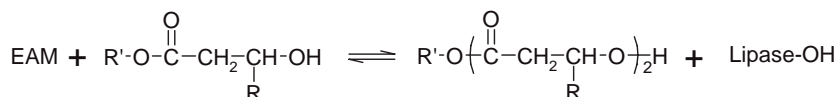
Initiation :



where, R' = H or alkyl group

R = H (β -propiolactone) or alkyl group (e.g. CH₃, β -butyrolactone derivatives)

Propagation :



Scheme 9.27 Postulated mechanism of lipase-catalyzed polymerization of β -lactones, illustrated by an alcohol initiator.

In 1993, Kobayashi *et al.* first reported the successful lipase-catalyzed ROP of lactones [82]. Although, initially only oligo-poly(BL) ($250 < M_w < 1050$) were prepared after several weeks using an equal quantity of lipase to BL monomers, some time later a much-improved enzyme-catalyzed polymerization of BL was reported which used thermophilic lipases to yield an optically active poly(BL) that was enriched with *R*-repeating units and had a M_w ranging from 900 to 3900 [83].

In addition to BL, the lipase-catalyzed ROP of substituted four-membered lactones such as β -methyl- β -propiolactone and β -propiolactone was first reported by Nobes *et al.* [84], followed by several studies with (\pm)- α -methyl- β -propiolactone [85], α -decenyl- β -propiolactone, α -dodecyl- β -propiolactone [86], and benzyl- β -D,L-malolactonate, among others [87].

As a general rule, depending on both lipase concentration and monomer conversion, the lipase-catalyzed polymerization of BL yields polymers having both cyclic and hydroxyl-terminated linear structures. As with other ionic and metallic coordinative processes, these structures are also 'contaminated' by the presence of crotonate end-groups [88]. The enzymatic polymerization of benzyl- β -D,L-malolactonate has been studied in bulk at 60°C in the presence of porcine pancreatic lipase (PPL) or immobilized *Candida antartica* lipase (Novozyme 435), whereupon poly(benzyl- β -D,L-malate) was produced with a weight-average molecular weight of 7200 and a polydispersity above 1.5. The polymerization of benzyl- β -D,L-malolactonate with *Candida rugosa* lipase yielded a slightly higher M_w of 8000 and a polydispersity of 1.4, and was therefore superior to immobilized *C. antartica* lipase in this respect. In order to gain a better insight into the mechanistic features of enzyme-catalyzed malolactonate polymerization, reactions with a β -substituted four-membered lactone (propyl malolactonate) were analyzed while varying the enzyme concentration, reaction medium composition and reaction temperature [89]. Although propyl malolactonate could be thermally polymerized, a significant increase in the rate of polymerization was observed when the reaction was carried out at 45 or 60°C in toluene, using *Candida rugosa* lipase (10wt%).

9.7

Illustrative Experimental Section

9.7.1

Anionic Ring-Opening Polymerization of Benzyl β -Malolactonate [27c]

To a previously flamed and nitrogen-purged round-bottomed flask is added 1.0 g (7.8 mmol) naphthalene, plus 0.37 g (9.5 mmol) potassium and 39 ml THF. After an overnight reaction, a deep green-colored solution of potassium naphthalene radical anion is obtained (concentration 0.2 mol l^{-1}). To another previously flamed and nitrogen-purged round-bottomed flask is added 0.52 g (1.97 mmol) 18-crown-6 ether and 0.43 g (1.97 mmol) 11-hydroxydodecanoic acid. These are dissolved in 10 ml of THF, after which a stoichiometric amount of the solution of potassium naphthalene radical anion (10.0 ml, 1.97 mmol, $[\text{HDD}] = 0.1 \text{ mol l}^{-1}$) is added. The polymerization of (*R,S*)-benzyl β -malolactonate (MLABz) (2.0 g, 9.7 mmol) is

typically conducted in a previously flamed and nitrogen-purged round-bottomed flask fitted with a three-way stopcock and a septum, by initiation with the complex formed between potassium 11-hydroxydodecanoate and 18-crown-6 ether (2.0 ml, 2.0×10^{-4} mol) in THF (44.5 ml) at 0°C. After 120 min, the polymerization is stopped by adding a few drops of aqueous HCl (0.1 mol l⁻¹). After evaporation of the solvent, the product is dissolved in dichloromethane (20 ml) and extracted three times each with a saturated aqueous KCl solution (3 \times 20 ml) and with deionized water (3 \times 20 ml). Finally, the organic layer is poured into 8 volumes of cold heptane (160 ml). The polymer is recovered by filtration and dried under reduced pressure at 40°C to constant weight (1.6 g).

- Yield: 79%.
- ¹H-NMR (300 MHz, CDCl₃, δ ppm,) 1.0–1.8 (m, 18H_b), 2.25 (t, 2H_c), 2.8 (m, 2H_e), 3.7 (t, 2H_a), 4.9–5.1 (s, 2H_f), 5.45 (m, H_d) and 7.3 (s, 5H_g).
- Gel permeation chromatography (GPC) analysis (with reference to polystyrene standards in THF at 35°C): $M_n = 7900$; $M_w/M_n = 1.2$.

9.7.2

Synthesis of Poly([R,S]- β -Butyrolactone), α -Methoxy, ω -Carboxylic Acid from Commercially Available 5-Methoxy-1,3,4-Triphenyl-4,5-Dihydro-1H-1,2-Triazol-5-Ylidene Carbene [78]

To a previously flamed and nitrogen-purged round-bottomed flask is added 50 mg (1.5×10^{-4} mol) commercially available 5-methoxy-1,3,4-triphenyl-4,5-dihydro-1H-1,2-triazol-5-ylidene. The material is purified (from an excess of methanol) and degassed at room temperature by three successive nitrogen/vacuum cycles. After treatment, 0.4 ml (4.99 mmol) of (R,S)- β -butyrolactone and 0.6 ml *t*-BuOH are added at room temperature ([BL]₀ \sim 5 mol l⁻¹). The polymerization is typically conducted at 80°C and stopped after 75 min by adding a few drops of carbon disulfide (CS₂). The medium is finally poured into 10 volumes of cold pentane (10 ml). The polymer is recovered by filtration and dried under reduced pressure at 50°C to constant weight (0.26 g).

- Yield 41%.
- ¹H-NMR (300 MHz, CDCl₃, δ ppm): 0.8–1.4 (d, 3nH), 2.1–2.5 (m, 2nH), 3.2 (s, 1H), 5.15 (m, nH).
- GPC analysis (with reference to polystyrene standards in THF at 35°C): M_n (size-exclusion chromatography) = 4150; $M_w/M_n = 1.19$.

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10

Polyesters from Dilactones

Odile Dechy-Cabaret, Blanca Martin-Vaca, and Didier Bourissou

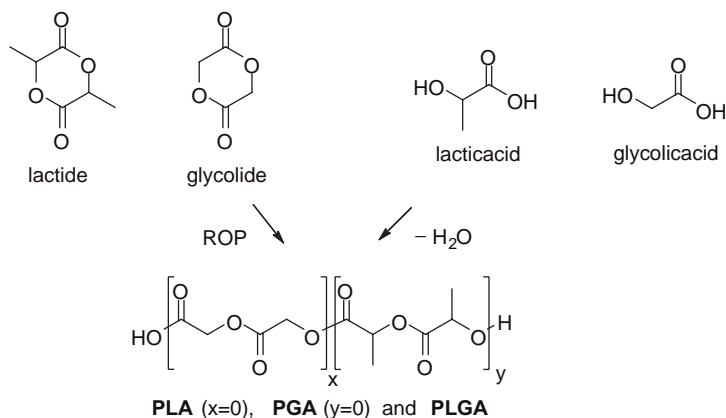
10.1

Introduction

The ring-opening polymerization (ROP) of dilactones has attracted considerable interest over the past few decades. Almost all of these investigations have focused on 1,4-dioxane-2,5-diones, and especially on lactide (LA) and glycolide (GA), the cyclic dimers of lactic and glycolic acids, respectively (Scheme 10.1).¹⁾ The resulting polyesters, which are commonly referred to as polylactide (PLA), polyglycolide (PGA) and related GA/LA copolymers (PLGAs), are both biodegradable (the aliphatic polyester backbone is sensitive to hydrolysis) and bioassimilable (hydrolysis releases glycolic and lactic acids—nontoxic compounds that are eliminated or assimilated via the Krebs cycle). Moreover, lactic acid—and thus lactide—can be obtained by the fermentation of renewable resources such as corn or sugar beet [1]. Based on these unique properties, PLGAs are at the forefront of research in synthetic polymers, and today are involved in applications in very different fields, ranging from surgery and pharmacology to packaging and textile fibers [2].

The practical uses of PLGAs are all dictated by their properties, and especially by their degradation rate and toughness, which can be tuned by modifying the structural parameters of the polymers. Accordingly, there is increasing interest in the development of new systems that allow for the preparation of PLGA polymers in a controlled manner and under mild conditions [2a–d]. In order to achieve this, two strategies have been proposed: (i) the step-by-step polycondensation of the α -hydroxyacids; and (ii) the ROP of the corresponding dilactones, which was pioneered as early as 1932 by W. Carothers (Scheme 10.1) [3]. The polycondensation route developed by Mitsui Chemicals suffers from the difficulty associated with water removal, and so permits only moderate control over the polymer microstructure. By comparison, the ROP of lactide and glycolide allows a much better control of polymerization in terms of molecular weight, polydispersity, monomer ratio

1) A few relevant studies have been reported regarding the ROP of macrocyclic dilactones, but only poly(α -hydroxyacids) deriving from 1,4-dioxane-2,5-diones and their equivalents are considered here.



Scheme 10.1 Lactide, glycolide, lactic, glycolic acids and their derived homo- and copolymers.

and sequence, polymer chain-ends and tacticity, and so is much more widely used. In this regard, it is striking to note that LA and GA are among the rare examples of polymerizable six-membered rings, with a polymerization enthalpy estimated at approximately 23 kJ mol^{-1} for lactide [4]. This peculiar behavior has been associated with the presence of two planar ester moieties within a skew-boat conformation [5]. However, the relief of ring strain, which provides the driving force for the ROP, remains modest so that the ROP thermodynamic equilibrium is not that favorable, especially at high temperature ($[\text{lactide}]_{\text{eq}} = 0.045 \text{ mol l}^{-1}$ at 20°C and 0.129 mol l^{-1} at 120°C) [4b]. This explains the numerous efforts devoted over recent decades to the development of catalytic systems that would promote the ROP of lactide under mild conditions and combine both efficiency and polymerization control.

In this chapter we present an overview of this increasingly active research field. The first section focuses on coordination polymerization with metal complexes, classified by the nature of their ancillary ligands. The spectacular achievements reported recently in organocatalyzed and stereocontrolled ROP are then presented. The third section concerns the macromolecular engineering of poly(α -hydroxyacids) by varying both their substitution pattern (with alternative monomers to lactide and glycolide) and their architecture (via block, star and dendritic copolymers). The well-established and rapidly emerging applications of these synthetic polyesters are discussed briefly in the last section.

10.2

General Concepts and ROP Promoted by Metallic Catalysts/Initiators

Tin(II) octanoate $[\text{Sn}(\text{Oct})_2]$, aluminum isopropoxide $\alpha\text{-Al}(\text{O}i\text{-Pr})_3$ and, to a lesser extent, zinc(II) lactate $[\text{Zn}(\text{Lact})_2]$ are the most widely used complexes (Figure 10.1). $\text{Sn}(\text{Oct})_2$ is inherently more active than $\text{Al}(\text{O}i\text{-Pr})_3$, with typical reaction times in bulk of a few hours versus a few days. $\text{Sn}(\text{Oct})_2$ is usually used in the presence

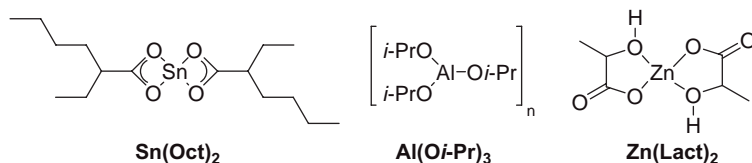
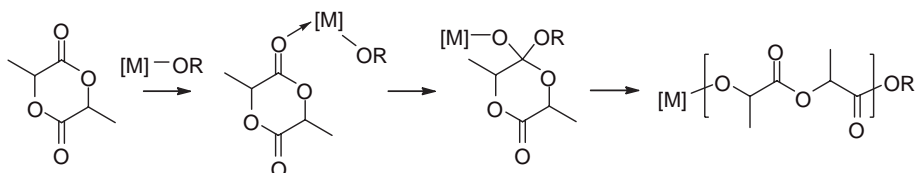


Figure 10.1 Structure of tin octanoate, aluminum isopropoxide and zinc lactate.



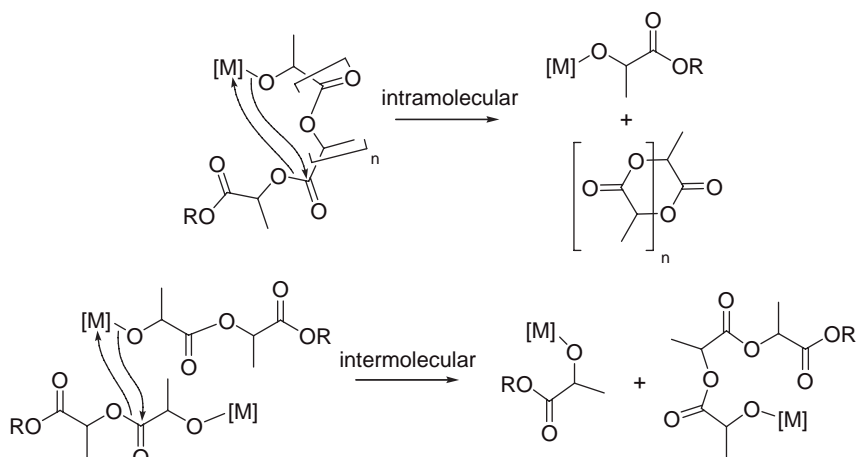
Scheme 10.2 Coordination–insertion mechanism for the metal-catalyzed ROP of lactide (RO refers either to the initiating alkoxy group or to the growing polymer chain).

of an alcohol as coinitiator, and affords polymers of high molecular weight (up to 10^5 – 10^6 g mol $^{-1}$) [6]. With $\text{Al}(\text{Oi-Pr})_3$, the polymerization systematically requires an induction period, which has been attributed to aggregation phenomena [7].

Both $\text{Sn}(\text{Oct})_2$ and $\text{Al}(\text{Oi-Pr})_3$ have been extensively studied in terms of activity, polymerization control and mechanism [8, 9]. According to experimental and theoretical data, the polymerization proceeds via a three-step coordination–insertion mechanism (Scheme 10.2). With $\text{Sn}(\text{Oct})_2$, the key alkoxide complex is generated *in situ* upon reaction with the exogenous alcohol. The nature of the ester chain-end is intimately related to the initiating alkoxide, and it is classically determined experimentally by ^1H NMR and/or mass spectrometry, using electrospray ionization (ESI) or matrix-assisted laser desorption ionization time-of-flight (MALDI-ToF) techniques. When all of the monomer has been consumed, the active metal–alkoxide bond is hydrolyzed and a hydroxyl end-group is liberated.

In such coordination–insertion polymerizations, the efficiency of the molecular weight control depends not only on the ratio $k_{\text{propagation}}/k_{\text{initiation}}$ but also on the extent of transesterification side reactions. These transesterification reactions can occur both intramolecularly (back-biting leading to macrocyclic structures and shorter chains) and intermolecularly (chain redistributions) (Scheme 10.3) [10]. The polymerization–depolymerization equilibrium should also be taken into account as a particular case of intramolecular transesterification reaction. All of these side reactions result in broader molecular weight distributions, and their extent was found to depend strongly on the metallic initiator. Typically, $\text{Sn}(\text{Oct})_2$ is much more active than $\text{Al}(\text{Oi-Pr})_3$ towards lactide, but the resulting PLAs exhibit significantly higher M_w/M_n values (ca. 2 versus 1.5 or less).

The promising results obtained with $\text{Sn}(\text{Oct})_2$, $\text{Al}(\text{Oi-Pr})_3$ and $\text{Zn}(\text{Lact})_2$ have stimulated the evaluation of a number of homoleptic complexes featuring alkoxy and carboxy ligands [2b]. As representative examples, trivalent yttrium and lanthanum alkoxides $\text{Ln}(\text{OR})_3$ ($\text{Ln} = \text{La}, \text{Y}$ and $\text{R} = i\text{-Pr}, n\text{-Bu}$) have proved to be much more active than the related aluminum alkoxides, and to efficiently promote the



Scheme 10.3 Intra- and inter-molecular transesterification side reactions.

ROP of lactide in solution at room temperature [11]. All of the experimental data support a coordination–insertion mechanism, with three active chains growing per metallic center; however, the practical use of these simple alkoxides may also suffer from aggregation phenomena [12].

Aiming at circumventing these problems, well-defined single-site catalysts have been of increasing interest over the past 20 years, and numerous studies have been devoted to enhancing their catalytic activity and limit the deleterious transesterification reactions. Such single-site catalysts can be represented by the general formula L_nMX , where M is the active metal center, X is an initiating group, generally an alkoxide, more rarely an amide, and L_n are ancillary ligands that are not directly involved in the polymerization but do tune the properties of the metallic center and minimize the aggregation processes and side reactions. On this basis, numerous complexes featuring different ancillary ligands (principally O -donors, N -donors and N,O -donors) have been reported to promote lactide ROP in a controlled manner via a coordination–insertion mechanism. An overview of the most relevant single-site catalysts is presented below.

10.2.1

O-Donor Ligands

Biphenolates and methylenebiphenolates have been evaluated as ancillary ligands for aluminum, zinc and lithium (Figure 10.2) [13–15]. Despite the presence of bulky groups in the *ortho* positions, all complexes exhibit dimeric structures or higher aggregates in the solid state. The dimeric Al and Zn complexes show much lower activity in the ROP of lactide (at least a few days at 80–110 °C are required to achieve good conversion) than the Li aggregates (complete conversion is obtained after only a few hours in dichloromethane, even at 0 °C). Polymers of molecular weights up to 14 000 g mol^{−1} and narrow distributions ($M_w/M_n \sim 1.1$) are obtained

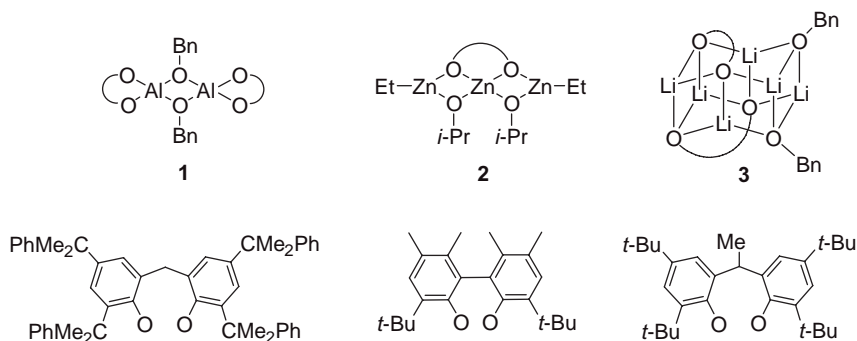
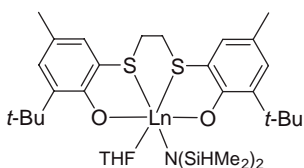


Figure 10.2 Representative Al, Zn and Li complexes featuring (methylene)biphenolate ligands.



Ln = Sc (**4a**), Y (**4b**), Lu (**4c**)

Figure 10.3 Rare earth metal complexes **4** featuring dichalcogen-bridged biphenolate ligands.

with these Li aggregates. The controlled character of the polymerization promoted by compound **3** supports a coordination–insertion mechanism rather than an anionic mechanism.

In order to prevent aggregation, additional neutral donor groups were introduced onto the ancillary ligands, as illustrated by the dichalcogen-bridged biphenolates [16]. These ligands were shown to have a strong beneficial effect towards lanthanides and Group III metals, the corresponding precursors $\text{Ln}[\text{N}(\text{SiHMe}_2)_2]_3(\text{THF})_x$ being less active and showing less control over the polymerization (Figure 10.3). In general, the less-hindered the metal center, the higher the activity for ROP of lactide. To date, the best results have been obtained by combining the yttrium complex **4b** with two equivalents of isopropanol: the ROP of lactide is complete after only a few minutes at room temperature in THF, and leads to narrowly distributed polymers ($M_w/M_n \sim 1.02$) of rather high molecular weights (ca. $20\,000\text{ g mol}^{-1}$).

10.2.2

N-Donor Ligands

With a view to achieving better control of the aggregation phenomenon commonly observed with oxygen-containing frameworks, nitrogen-based ligands have been widely studied. The additional substituent at the nitrogen compared with oxygen was expected to result in more steric hindrance, and the ensuing N–metal bonds were supposed to be inert towards monomer insertion, at least in the presence of a highly active initiating group such as an alkoxy moiety.

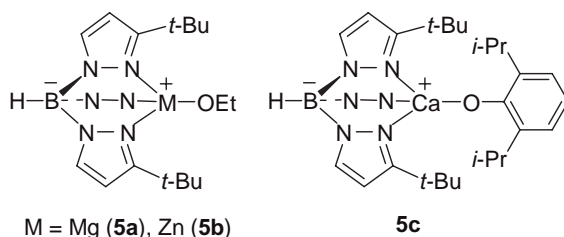


Figure 10.4 Representative Mg, Ca and Zn complexes featuring trispyrazolyl-hydroborate ligands.

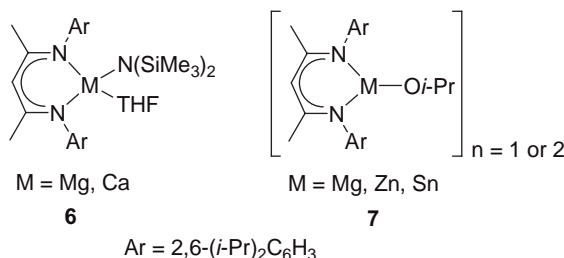


Figure 10.5 Representative Mg, Ca, Zn and Sn complexes featuring β -diiminate ligands.

The tripodal trispyrazolyl-hydroborate ligands produce sufficient steric hindrance around the metallic center to prevent aggregation, as exemplified by the monomeric magnesium, zinc and calcium complexes **5a–c** (Figure 10.4) [17]. Most of these complexes were highly active for lactide ROP, with the observed reactivity order $\text{Ca} > \text{Mg} > \text{Zn}$ having been attributed to the difference in polarity of the initiating M–O bonds.²⁾ The calcium derivatives **5c**, which are capable of polymerizing 100 equiv. of lactide in only 1 min at room temperature in THF, are among the most active complexes discovered to date [17b]. However, the inverse trend is observed for the molecular weight distributions of the resulting polymers, calcium derivatives leading to higher polydispersity indexes (ca. 1.6–1.7) than magnesium and zinc initiators (ca. 1.1–1.25).

β -Diiminate complexes of divalent metals, mainly zinc and magnesium, but also calcium, tin and iron(II), have also been evaluated for the ROP of lactide (Figure 10.5) [17b,c, 18]. The nitrogen substituents pointing towards the bonded center provide efficient steric hindrance so that monomeric or dimeric structures are observed in the solid state. All of the complexes **6** and **7** were shown to catalyze lactide ROP efficiently in dichloromethane (DCM) at room temperature. For complexes bearing an alkoxide initiating group, comparative studies have suggested the reactivity order $\text{Mg} > \text{Zn} \approx \text{Fe} > \text{Sn}$ [17b,c, 18], which parallels the electropositivity of the metal. So far, related calcium complexes have only been obtained with amido coligands (disproportionation reactions are observed with alkoxides) and the reverse reactivity order $\text{Ca} < \text{Mg}$ observed in this series was tentatively attributed to aggregation phenomena [17c].

2) Pauling electronegativities are as follows: calcium (1.0), magnesium (1.2) and zinc (1.6).

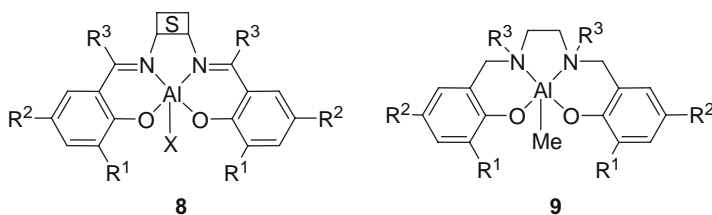


Figure 10.6 General structure of Al complexes featuring SALEN and SALAN ligands (S = spacer).

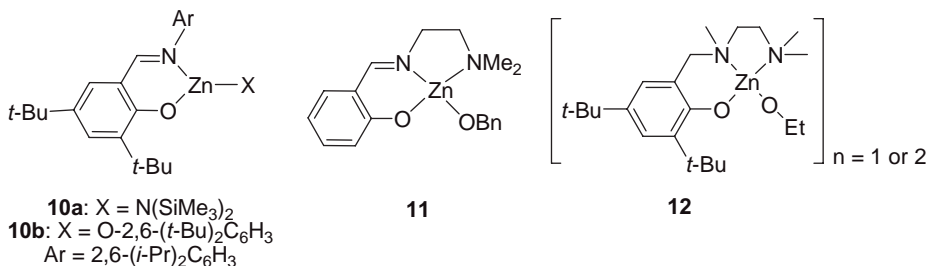


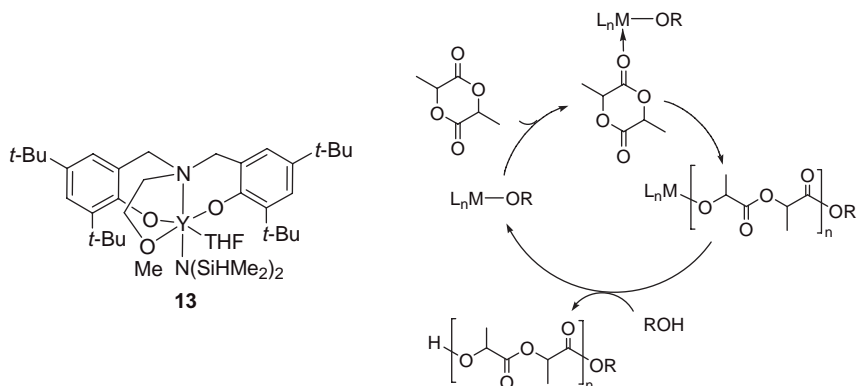
Figure 10.7 Zn complexes featuring half-SALEN and diamino-phenolate ligands.

10.2.3

N,O-Donor Ligands

Chelating ligands combining N- and O-donors have also been involved in the design of well-defined complexes for the ROP of lactide, and numerous studies have been devoted to aluminum complexes **8** derived from SALEN ligands (Figure 10.6) [19]. All of these complexes proved only moderately active (high conversions typically require a few days at 70 °C in toluene), but the polymerizations were well controlled. The initiating alkoxide coligand was directly incorporated at aluminum or generated *in situ* by the alcoholysis of alkyl aluminum precursors. The versatility and accessibility of the SALEN ligands have favored extensive modifications of steric and/or electronic properties of the aryl and imino substituents, as well as the flexibility of the spacer [19]. These studies have been further expanded to the related saturated SALAN complexes **9** [20]. The stereocontrolled ROP of lactide with (a)chiral SALEN- and SALAN-based aluminum complexes has also been reported (see Section 10.2.2).

Chisholm and coworkers recently initiated the investigation of complexes derived from bulky Schiff bases (i.e. half-SALEN ligands) as N,O analogues of β -diiminates [21]. The bulky phenoxide coligand ensures a monomeric structure for **10b** in the solid state, but at the expense of its activity towards ROP of lactide which is even lower than that of the amido complex **10a** (Figure 10.7). An amino side-arm was introduced at the Schiff base ligand, so that monomeric structures could be retained even with smaller alkoxide initiating groups (complexes **11**), and higher activities could be achieved (complete conversion within 30 min at room temperature) [22]. A related phenolate-based ligand featuring a single ethylene-diamine arm



Scheme 10.4 Selected Y complex featuring a methoxy-amino-biphenolate ligand and schematic representation of *catalytic* ROP based on alcohol exchange reactions (RO refers to the exogenous alkoxy group or to the growing polymer chain).

has also been studied by Hillmyer and Tolman. The zinc ethoxide complex **12** was found to be dimeric in the solid state, but essentially monomeric in solution [23]. Using this complex, lactide was polymerized at a rate faster than with any other Zn-containing system reported so far (in DCM at room temperature, the rate constant for ROP of lactide with **12** is 5.1-fold higher than with the β -diiminate derivative **7**, and 1220-fold higher than with the trispyrazolyl-hydroborate derivative **5**) [23]. Polylactides with molecular weights as large as $130\,000\text{ g mol}^{-1}$ and relatively low polydispersity indexes ($M_w/M_n \sim 1.4$) were obtained in this way.

Finally, aminobiphenolate ligands featuring a pendant amino or ether group have been coordinated to Group III metals and lanthanides (Scheme 10.4) [24]. With all of these complexes, the ROP of lactide proceeds within a few minutes at room temperature in toluene or THF, and the polymerization is well controlled [24b]. Taking advantage of these very high activities, catalytic amounts (down to 0.02 mol%) of the metal complex **13** relative to isopropanol (as the exogenous initiating alcohol) could be used, and polymers with predictable M_n and low polydispersity indexes (<1.2) were obtained. Such *catalytic* ROP relies on fast alcohol/alkoxide exchange reactions at the metal, and enables the production of large quantities of polymers with only small amounts of metal complexes [24c].

10.3

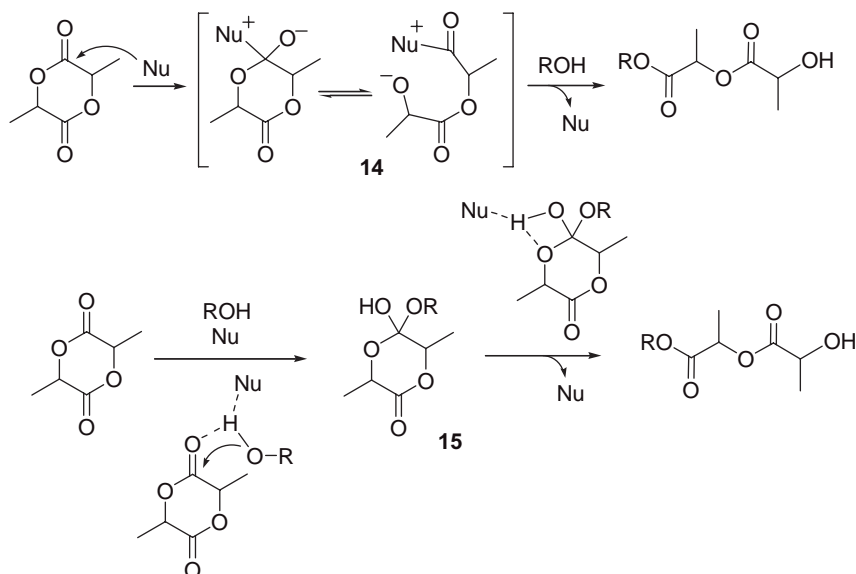
Recent Advances in ROP

10.3.1

Metal-Free ROP

10.3.1.1 Nucleophilic/Basic Catalysts

Pyridines [25], *N*-heterocyclic carbenes (NHCs) [26] and, more recently, phosphazenes [27] have all proved to be efficient catalysts for the ROP of lactide



Scheme 10.5 Nucleophilic/basic pathways for the ROP of lactide. (Nu = amine, *N*-heterocyclic carbene or phosphazene, ROH = the initiating protic agent or the growing polymer chain).

[28].³⁾ Most of these polymerizations require a protic initiator ROH that dictates the nature of the α -chain-end of the resulting PLAs (typically an acid or ester functionality). Although the mode of action of these organocatalysts is not precisely known, the polymerization most probably occurs via nucleophilic activation of the monomer (involving a transient lactide–catalyst complex 14) and/or base-catalyzed transesterification (involving a transient tetrahedral adduct 15) (Scheme 10.5) [29]. The controlled character of the polymerization has been established for all organocatalysts by a linear correlation between the molecular weight of the polymer and the monomer conversion. As a consequence, the degree of polymerization closely tracks the initial monomer-to-initiator ratio, and PLAs of controlled molecular weights and narrow distributions are obtained.

4-Aminopyridines, such as 4-dimethylaminopyridine (DMAP), were the first nucleophilic organocatalysts to be used for the polymerization of lactide [25]. High monomer conversions were achieved after a few days in refluxing DCM and after a few minutes in bulk (135 °C). Notably, prolonged heating at 35 °C does not induce detectable changes in molecular weight and polydispersity, indicating that undesirable side reactions are less operative with pyridine catalysts than with metal complex initiators.

These preliminary results then motivated the investigation of NHCs as organocatalysts for lactide ROP, and the representative imidazol-2-ylidene IMes

3) The feasibility and potential of enzyme-catalyzed lactide polymerization in organic solvents have been demonstrated, but enzymes

are not yet capable of competing with metal-based initiators or organocatalysts in terms of reaction time and polymerization control [2d].

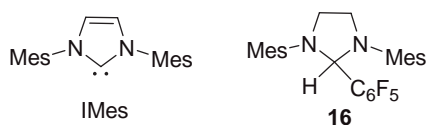
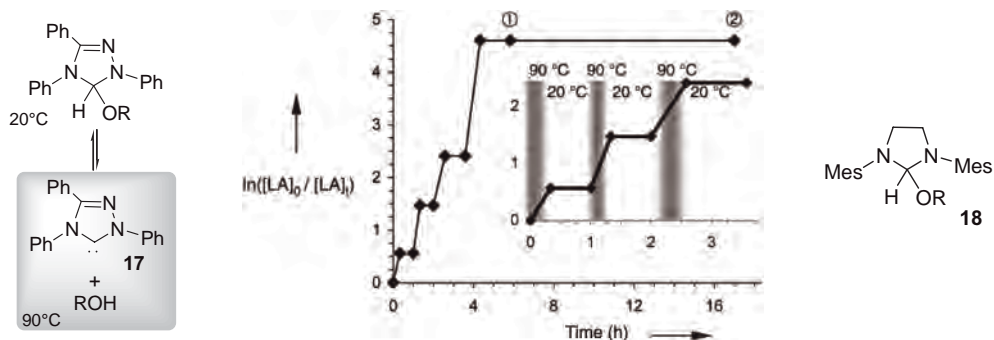


Figure 10.8 Structures of the representative *N*-heterocyclic carbene IMes (Mes = 2,4,6-Me₃C₆H₂) and of the thermally labile adduct **16**.

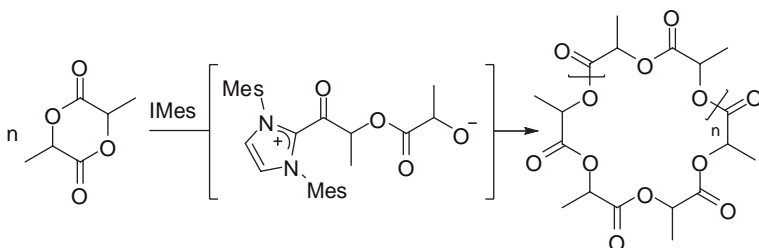
(Figure 10.8) proved to be extraordinarily active, with complete monomer conversion being typically achieved in less than 1 h at room temperature to afford PLAs of high and controlled molecular weights [26a, 30]. Careful control of the catalyst-to-initiator ratio and lactide concentration is needed in order to obtain precisely controlled and narrowly distributed molecular weights, and the optimal conditions proved to be rather carbene-dependent. From a practical viewpoint, biphasic THF/ionic liquid systems allow: (i) the generation *in situ* of the organocatalyst using 1-ethyl-3-methylimidazolium tetrafluoroborate [emim][BF₄] as an NHC reservoir; (ii) easy and quantitative recovery of the resulting PLAs from the THF phase; and (iii) recycling of the liquid ionic phase [30b]. Alternative methods for generating the NHC catalyst *in situ* were investigated, especially from thermally activated NHC adducts. Here, the pentafluorophenyl imidazolidine **16** was the preferred carbene source as it combines room-temperature stability (both in solid state and in solution) with good activity, even upon moderate heating (high monomer conversions require a few hours at 65 °C) (Figure 10.8) [31]. From a practical viewpoint, however, the use of such imidazolidine adducts is limited by lactide racemization (eventually observed during polymerization).

Further studies demonstrated the ability of alcohol adducts of NHCs to act as ‘all-in-one’ catalyst/initiators [32, 33]. These developments were stimulated by the propensity of the triazol-2-ylidene **17** to form stable adducts with alcohols. In taking advantage of the reversible character of this O–H insertion reaction, the polymerization was carried out at 90 °C with various alcohols as initiators. A temperature switch could be operated by alternating high (90 °C) and low temperatures (20 °C), either activating or deactivating the ROP of lactide (Scheme 10.6). Accordingly, the formation of a dormant form of the catalyst with the initiating/propagating alcohol allows precise control of the concentration of the active species, thereby limiting adverse side reactions. Variation of the NHC structure allowed further improvement of this approach, and culminated in the development of alcohol adducts that function as ‘all-in-one’ catalyst/initiators under mild conditions [33]. Indeed, both primary and secondary alcohol adducts of the imidazolin-2-ylidene **18** were found to be stable solids that readily and reversibly dissociate in solution at room temperature. Under these conditions, the ROP of up to 100 equiv. of lactide requires less than 15 min and affords well-controlled PLAs [33].

A further breakthrough was recently reported by Hedrick and Waymouth, who used NHCs to promote the polymerization of lactide in the absence of protic initiators [34]. Under these conditions, zwitterionic polymerization readily occurs to provide cyclic PLAs with rather narrow distributions ($M_w/M_n \sim 1.3$) and a remark-



Scheme 10.6 Alcohol adducts of NHCs as single-component catalyst/initiator and temperature switch of the lactide ROP by alternating high (90 °C) and low (20 °C) temperatures. (ROH = primary or secondary initiator or propagating chain). (Reproduced with permission from Ref. [32a].)



Scheme 10.7 Zwitterionic polymerization of lactide to cyclic PLAs using an NHC.

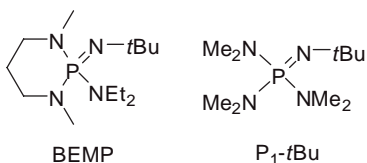
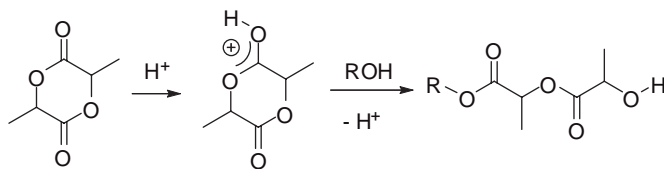


Figure 10.9 Structures of the phosphazene bases used to promote the pseudoanionic ROP of lactide.

able degree of control (Scheme 10.7). The selective formation of high-molecular-weight macrolactones is consistent with the initiation rate being slower than the propagation rate. The presence of both even and odd numbers of lactate units deduced from MALDI-TOF analyses indicates that the propagating zwitterionic polymers and/or their cyclic forms readily undergo transesterification reactions. Finally, gel permeation chromatography (GPC) analyses coupled with a light-scattering detector and a viscometer allowed for comparison of the properties of cyclic and linear samples of similar molecular weights. As expected, lower intrinsic viscosities and hydrodynamic radii were observed for the macrocyclic structures.

The variety of active organocatalysts has been recently further extended to phosphazene bases, with both BEMP and P_1 -*t*Bu (Figure 10.9) promoting the ROP of lactide within a few days in solution at room temperature in the presence of an initiating alcohol [27]. Quenching the organocatalyst with benzoic acid is necessary to prevent undesirable transesterification reactions and to achieve narrow



Scheme 10.8 Activated-monomer pathway for the cationic ROP of lactide. (ROH = the initiating protic agent or the growing polymer chain).

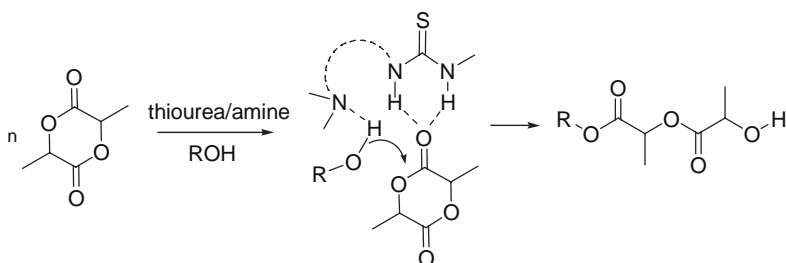
molecular weight distributions. Preliminary mechanistic studies support a pseudoanionic pathway, with the phosphazene acting as a base to activate the initiating/propagating alcohol and to facilitate the proton transfer. The efficiency and versatility of this approach was further demonstrated by chain extension of hydroxyl-functionalized macroinitiators, leading to block copolymers.

10.3.1.2 Cationic Polymerization

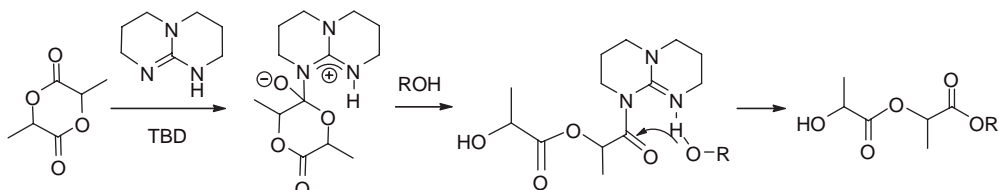
The ability of HX/ROH combinations to promote ROP was first evidenced by Endo and Jérôme towards δ -valerolactone and ϵ -caprolactone [35], and further extended to lactide by Bourissou [36, 37]. Accordingly, the cationic polymerization of lactide can be achieved in solution within a few hours at room temperature using trifluoromethanesulfonic acid (HOTf). The controlled character of the polymerization was substantiated by: (i) the quantitative incorporation of the protic initiator; (ii) the presence of only even lactate units in the resulting polymers, demonstrating that transesterifications do not occur to a significant extent during the polymerization; (iii) the absence of stereoerror during the polymerization of L-lactide, indicating negligible, if any, epimerization (for stereocontrol in ROP of lactide, see Section 10.3.2), despite the strong acidic character of HOTf; and (iv) the linear relationships $M_n = f([M]_0/[I]_0)$ and $M_n = f(\text{monomer conversion})$. In addition, the ‘living’ character of the polymerization was evidenced by a second-feed experiment, while kinetic studies revealed a first-order dependence on LA (k_{obs} of $6.8 \times 10^{-3} \text{ min}^{-1}$ at room temperature). All of these data support an activated-monomer cationic polymerization (Scheme 10.8) [38]. Although HOTf clearly does not compete with NHCs in terms of activity, it slightly surpasses DMAP and combines ready availability and ease of removal [39].

10.3.1.3 Bifunctional Catalysts

The spectacular achievements reported in organic synthesis through the cooperative activation of several reaction partners have stimulated the investigation of multicenter catalysis for the ROP of lactide [40]. This new metal-free approach to PLAs was pioneered by Waymouth and Hedrick, using a combination of thiourea and tertiary amine moieties for dual hydrogen-bonding of the monomer and initiating/propagating alcohol (Scheme 10.9) [41]. Accordingly, efficient and very well-controlled polymerizations were achieved with ‘two-in-one’ catalysts, although long reaction times were required under typical conditions (a few days at room temperature for a catalyst loading of 5 mol%). Variations of the linkage between the thiourea and amine functionalities did not bring about any enhanced activities,



Scheme 10.9 Dual activation of lactide and alcohol (ROH = initiator or propagating chain) by the thiourea/amine combination.



Scheme 10.10 Dual activation of lactide and alcohol (ROH = initiator or propagating chain) by the guanidine catalyst TBD.

but further investigations showed that the thiourea and amine did not have to be assembled in a ‘two-in-one’ system to promote the efficient ROP of lactide. Accordingly, the two partners could be varied over a broader range of structures, and significantly higher catalytic activities obtained through the careful optimization of steric and electronic effects. So far, the best results have been obtained by combining the thiourea $\text{CyNHC}(=\text{S})\text{NHAr}_\text{F}$ [$\text{Ar}_\text{F} = 3,5\text{-(CF}_3)_2\text{C}_6\text{H}_3$] and sparteine, with complete monomer conversions being achievable in only a few hours at room temperature, even with lower catalyst loadings (1.5–2.5 mol%). When separate thiourea and amine were used, stereoerrors attributable to monomer epimerization could be detected in the homopolymerization of L-lactide, but their extent remained limited (4%) for the lead combination $\text{CyNHC}(=\text{S})\text{NHAr}_\text{F}$ /sparteine. In addition, the efficiency and functional group tolerance of such thiourea–amine bifunctional catalysts have been substantiated by the preparation of various end-capped PLAs, as well as block copolymers [41b].

The commercially available guanidine 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) proved to be more active for the ROP of lactide than any other organocatalyst, even competing with the most efficient metal systems [42]. Typically, complete polymerization was achieved in only a few minutes at room temperature, while the guanidine catalyst could be quenched by addition of benzoic acid to prevent any adverse transesterification reactions. From a mechanistic viewpoint, the strongly basic TBD ($\text{pK}_\text{aH} = 26.0$ in MeCN) may be anticipated to deprotonate, or at least activate, the initiating/propagating alcohol. However, both the N-methylated analogue of TBD and amidine 1,5-diazabicyclo(5,4,0)undec-5-ene (DBU) were found to be much less active, despite having only slightly lower basicities. This suggests a dual activation mechanism with TBD (as depicted in Scheme 10.10) rather than

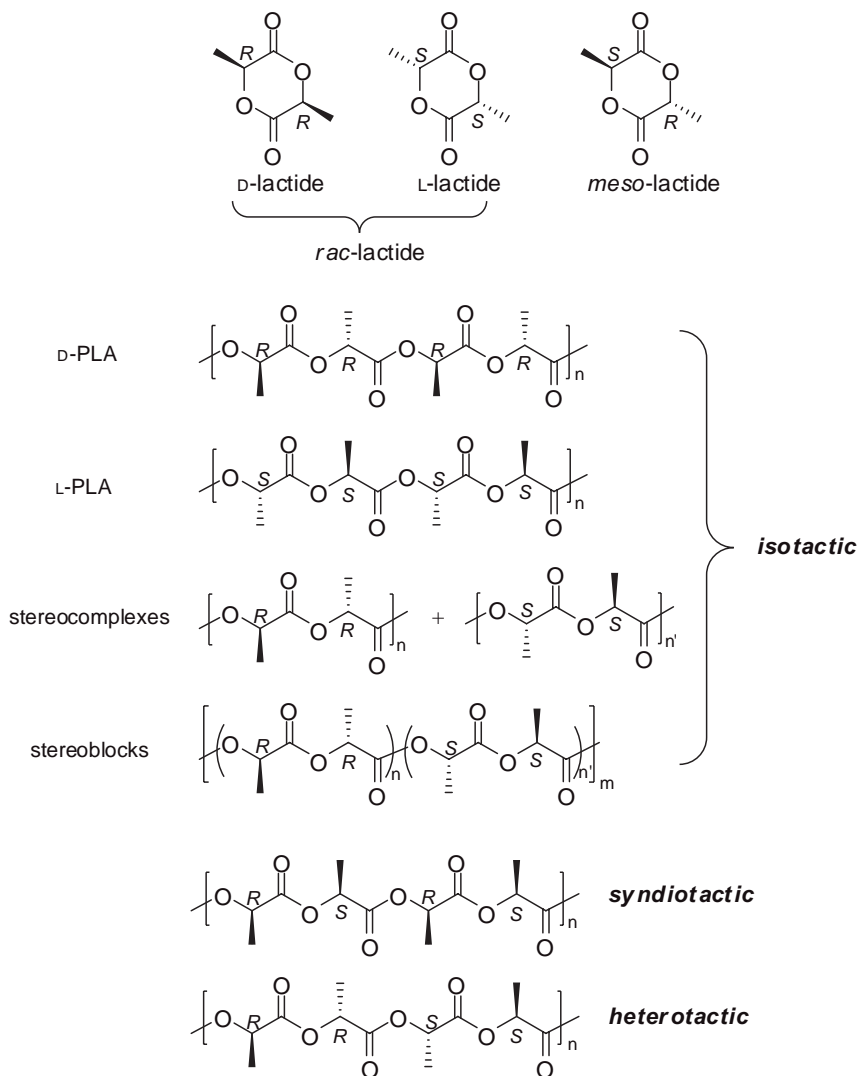


Figure 10.10 *meso*- and *rac*-lactide and the different stereoregular polylactides.

a simple pseudoanionic pathway [43]. In marked contrast to most of the catalysts reported so far, TBD depicted high selectivity for lactide over other lactones (such as δ -valerolactone, ϵ -caprolactone and β -butyrolactone), opening the way to block copolymers.

10.3.2

Stereocontrolled ROP

Lactide can be found as L-lactide, D-lactide, the racemic mixture thereof (namely *rac*-lactide), and *meso*-lactide. Polylactides can thus exhibit different microstruc-

Table 10.1 Stereoregular PLAs expected from pure site-controlled and chain-end-controlled ROP of *rac*- and *meso*-lactide.

	Site control (metal catalyst)	Chain-end control (metal and organic catalyst)
<i>rac</i> -Lactide	Isotactic	Isotactic or heterotactic
<i>meso</i> -Lactide	Syndiotactic ^a	Syndiotactic or heterotactic

^a Assuming that no exchange reactions occur at the metal.

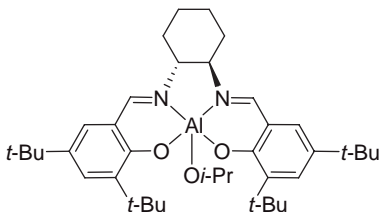
tures (isotactic, syndiotactic and heterotactic), depending both on the monomer involved and on the course of the polymerization reaction. It should be noted that the term ‘isotactic PLAs’ refers not only to pure L-PLA and D-PLA, but also to the corresponding stereocomplexes and stereoblocks (Figure 10.10).

The stereosequence distribution in PLA samples is usually determined by NMR spectroscopy through inspection of the methine region in homonuclear decoupled ¹H NMR or the carbonyl region in proton-decoupled ¹³C NMR. The stereoselectivities are classically quantified by P_m and P_r values associated with the probabilities of *meso* and *racemic* linkage between monomer units, respectively.

The physical properties of polylactides depend heavily on their stereochemical composition, with stereoregular crystalline polylactides exhibiting high melting temperatures in contrast with atactic amorphous polymers.⁴⁾ Of particular interest, high melting temperatures are not restricted to enantiomerically pure L- and D-PLA ($T_m \sim 180^\circ\text{C}$), and are even surpassed by PLA stereocomplexes (T_m up to 230°C) [44] and PLA stereoblocks (T_m up to 205°C) [45]. From a practical viewpoint, high T_m values allow higher use temperatures for the PLAs, and thereby broaden their range of applications. Stereoregular crystalline PLAs are thus particularly attractive targets, and single-site catalysts have stimulated numerous investigations in this context, as valuable alternatives to conventional catalysts [Sn(Oct)₂, Zn(Lact)₂, Al(Oi-Pr)₃] that usually lead to atactic polymers from *rac*-lactide.

Efficient stereocontrolled ROP requires catalytic systems which induce negligible, if any, transesterification reactions. From a fundamental viewpoint, two different pathways can be distinguished in the stereocontrolled ROP of *rac*- and *meso*-lactide with single-site catalysts: (i) a chain-end control mechanism in which the last unit in the growing polymer chain influences which enantiomeric form of the monomer is incorporated next; and (ii) an enantiomorphous site control mechanism in which the chirality of the catalyst defines the stereochemistry of the monomer insertions (Table 10.1). To date, site control has only been evidenced in coordination–insertion polymerizations, taking advantage of the covalent linkage of the monomer and growing polymer chain to the metal center. As far

4) For instance, pure isotactic poly-(L-lactide) is a highly crystalline material ($T_m \sim 180^\circ\text{C}$), whereas related random copolymers featuring 15% of *meso*-lactide are amorphous with a T_m of only 130°C (see Ref. [1]).



rac-8a: 70 °C, toluene, stereoblocks, T_m , 179 °C

rac-8b: 70 °C, toluene, stereoblocks, P_m 0.93, T_m 183 °C

complexes leading to

Figure 10.11 Chiral SALEN–aluminum complexes leading to isotactic PLAs by site-controlled ROP of *rac*-lactide.

as chain-end control is concerned, high stereoselectivities could be obtained from sterically encumbered catalytic sites, using not only metal complexes but also organocatalysts. It should be noted that with chiral complexes both site and chain-end control mechanisms may intervene so that the precise factors controlling the overall stereoselectivity are usually difficult to determine [46].

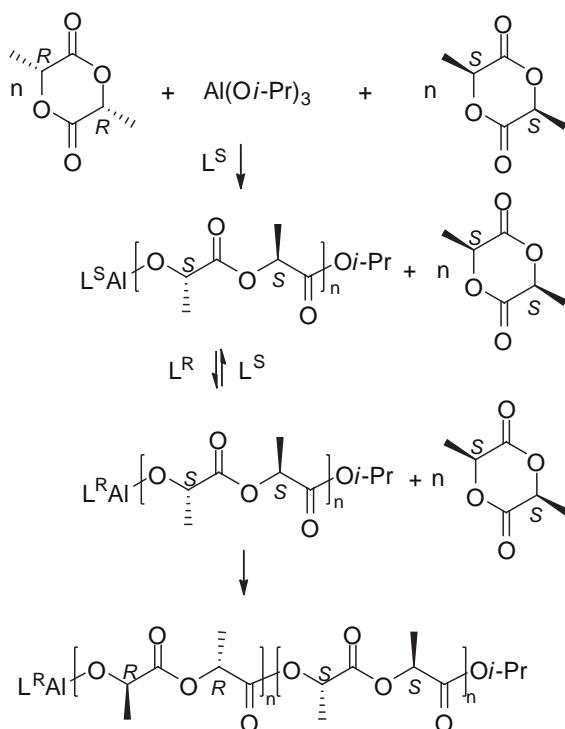
The various approaches to stereoregular PLAs will be illustrated below. Representative P_m and P_r selectivities will be provided along with polymerization conditions and, when available, T_m values for isotactic PLAs.

10.3.2.1 rac-Lactide

The site control strategy was first investigated by the kinetic resolution of *rac*-lactide with chiral aluminum complexes featuring SALEN ligands derived from (*R,R*)-binaphthyldiamine [19f] and (*R,R*)-cyclohexanediamine [19d] (Figure 10.11). Under these conditions, the preferential polymerization of L- or D-lactide affords enantiomerically enriched isotactic polymers only at low monomer conversions. For higher conversions, the enrichment of the monomer pool of the ‘wrong isomer’ results in polylactides with gradient L-lactide/D-lactide ratios within the polymer chains. However, when the racemic catalysts **8a** and **8b** are used instead of the homochiral catalysts, the parallel site stereocontrolled synthesis of isotactic poly(D-lactide) and poly(L-lactide) from *rac*-lactide can be achieved as the D/L ratio in the monomer pool remains constant during the polymerization. Detailed NMR studies launched by Coates [19e,f] and Feijen [19d] demonstrated that stereoblocks rather than stereocomplexes were obtained, which suggests that exchange reactions of the growing polymer chains occur at the metal centers.

Duda *et al.* reported another elegant approach to PLA stereoblocks by combining site control and chiral ligand-exchange (Scheme 10.11) [19g]. High-melting polylactides (T_m up to 210°C) were obtained via consecutive site-controlled polymerization of both enantiomers of *rac*-lactide, with the homochiral ancillary ligand rapidly exchanging with its enantiomer after half conversion.

Alternatively, chain-end-controlled ROP of *rac*-lactide leading to isotactic PLA stereocomplexes has been demonstrated with achiral SALEN-, SALAN- or homo-SALEN-based aluminum complexes. An exploration of various ligands has begun



Scheme 10.11 Two-step polymerization of *rac*-lactide combining stereoselection and chiral ligand exchange. L^S and L^R denote the SALEN ligands derived from salicylaldehyde and (*S,S*)- and (*R,R*)-binaphthyldiamine, respectively.

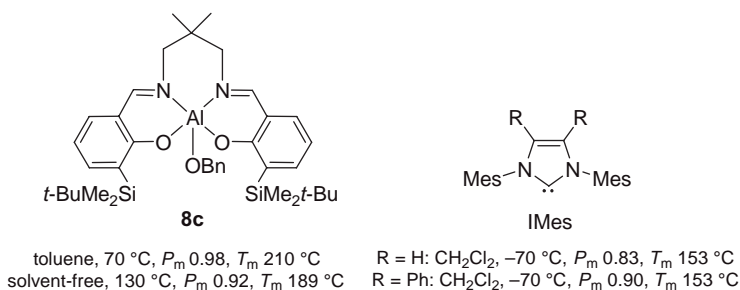


Figure 10.12 Achiral catalysts leading to isotactic PLAs by chain-end-controlled ROP of *rac*-lactide.

[19b,c,h, 47], and the best stereoselectivities so far (including an attractive solvent-free process) were reported for complex **8c** (Figure 10.12). This approach has also been developed with metal-free systems, where good selectivities were achieved with the sterically encumbered N-heterocyclic carbenes IMes at low temperature [48]. Strikingly, a related Zn alkoxide catalyst featuring an IMes ligand showed the opposite stereoselectivity, yielding heterotactic PLAs [48b].

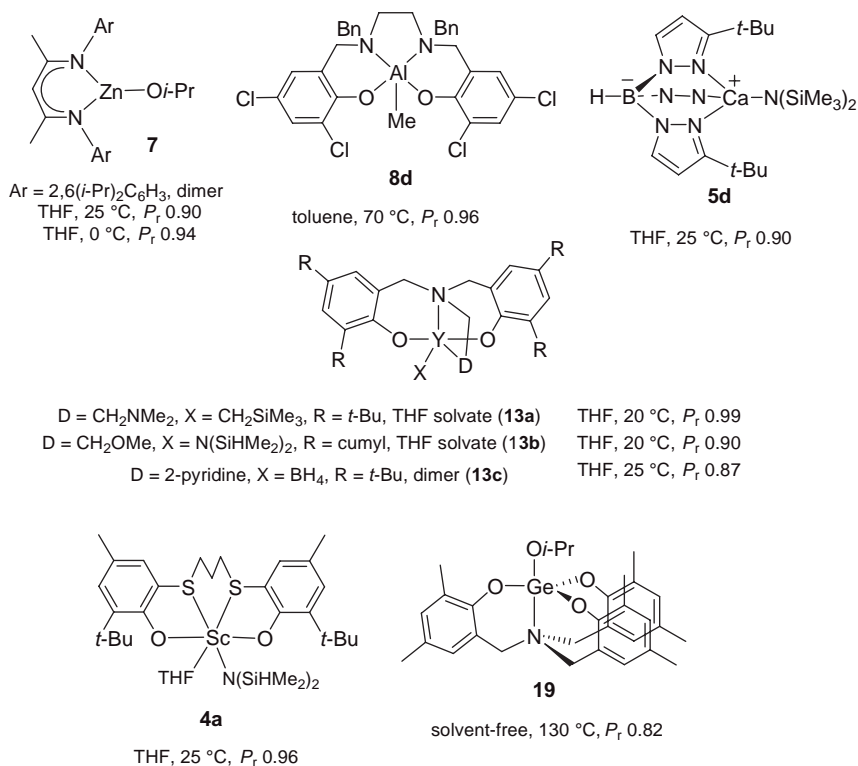


Figure 10.13 Metal complexes leading to heterotactic PLAs by chain-end-controlled ROP of *rac*-lactide.

The chain-end-controlled ROP of *rac*-lactide was more frequently found to afford heterotactic PLAs, as reported with the β -diiminate–Zn complex **7** [18a–c, 49], SALAN–Al complex **9** [20], trispyrazolyl-hydroborate–Ca complex **5d** [17b,c] and bis-phenolate Group III complexes **4** [16c] and **13** [24, 50, 51] (Figure 10.13). On the basis of sterically encumbered ancillary ligands, P_r selectivities of up to 96–99% were obtained at temperatures ranging from 20 to 70 °C. Preliminary investigations suggested that the substitution pattern of the ligand and the nature of the central metal strongly influenced the stereocontrol, as well as the polymerization conditions (solvent, temperature). A promising result in solvent-free stereocontrolled ROP has also been reported recently with an original Tris-phenolate–Ge complex **19** [52]; the precise role of the C_3 -symmetry in this case remains to be determined.

10.3.2.2 *meso*-Lactide

A few examples of syndiotactic PLA preparations have been reported by the site-controlled ROP of *meso*-lactide with chiral complexes. Whilst only moderate selectivities were obtained with the trisindazolyl-hydroborate–magnesium complex **20** (Figure 10.14) [17a], better results were achieved with the SALEN–aluminum complex **8a** (toluene, 70 °C, P_r 0.96) [19e]. Strikingly, the enantiomerically pure

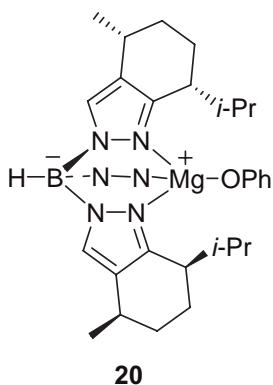
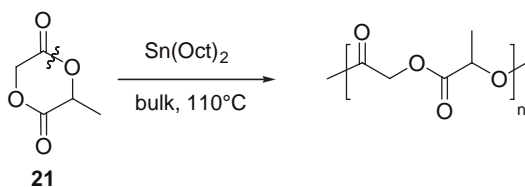


Figure 10.14 Trisindazolyl-hydroborate magnesium complex **20** leading to syndiotactic PLAs by site-controlled ROP of *meso*-lactide.



methylglycolide

Scheme 10.12 Preparation of poly(lactide-*alt*-glycolide) from methylglycolide **21**.

form of this catalyst led to syndiotactic PLAs, whereas its racemic form gave heterotactic PLAs [19e]. To date, the exact nature of the stereochemical control has remained unclear, but exchange reactions are most likely involved.

A chain-end-stereocontrolled polymerization of *meso*-lactide was also observed, the bulky achiral β -diiminate-zinc complex **7** [18b] leading to syndiotactic PLAs (CH_2Cl_2 , 0°C , P_r 0.76) and N-heterocyclic carbenes IMes leading to heterotactic PLAs (P_r up to 0.83 at -40°C) [47b].

10.4

Macromolecular Engineering

10.4.1

'Modified' PLGAs: Alternative Monomers to Lactide and Glycolide

In order to tune and further broaden the properties of poly(α -hydroxyacids), the homopolymerization and copolymerization of various substituted 1,4-dioxane-2,5-diones have been studied.⁵⁾ In particular, the polymerization of methylglycolide **21** was investigated, aimed at preparing alternating copolymers of lactide and glycolide based on the preferential ring opening of at least the sterically hindered acyl moiety (Scheme 10.12) [53].⁶⁾ Although this strategy could be validated with

5) The different synthetic routes to symmetrically and dissymmetrically substituted 1,4-dioxane-2,5-diones have been recently reviewed (see Ref. [2d]).

6) This selectivity is supported by the higher reactivity of glycolide versus lactide ($r_G/r_L \sim 10$).

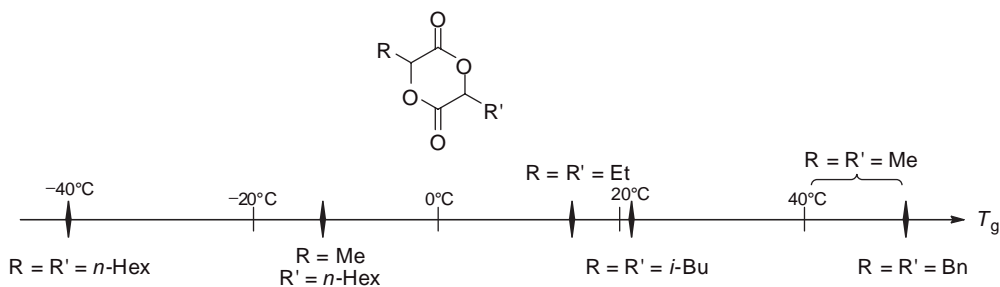


Figure 10.15 Substituted 1,4-dioxane-2,5-diones and T_g of the corresponding homopolymers.

$\text{Sn}(\text{Oct})_2$ as a catalyst, further developments have so far been limited by the poor availability of the crossed dimer **21** (obtained in two steps and 43% overall yield from glycolic acid and 2-bromopropionyl bromide) [53b, 54].

The homopolymerization of 1,4-dioxane-2,5-diones substituted with alkyl or benzyl groups has also been performed in bulk with $\text{Sn}(\text{Oct})_2$ in order to modulate the physical and chemical properties of poly(α -hydroxyacids) (Figure 10.15) [55]. Accordingly, the introduction of pendant linear alkyl groups was found to lower the glass transition temperature (T_g) down to -40°C by internal plasticization, whereas branched alkyl groups resulted in a higher T_g due to a restricted mobility of the polymer backbone. Preliminary investigations have also been carried out regarding the influence of the pendant group on the hydrolytic degradation of the polymers [55b,d].

Substitution of the 1,4-dioxane-2,5-dione ring presents an opportunity to prepare polyesters featuring functional side groups [56–58]. Here, protected monomers **22–26** derived from malic acid, D-gluconic acid, glyceric acid, glutamic acid and lysine have been prepared and polymerized. The steric factors were shown to play a prominent role, and the monomers **22a–24a** featuring a sterically released glycolate unit were much more readily polymerized, affording perfectly alternating copolymers⁷⁾ as deduced from ^1H and ^{13}C NMR analyses (Figure 10.16). The pendant functional groups can be deprotected without affecting the polymer backbone, via catalytic hydrogenolysis or acidic hydrolysis. The presence of pendant carboxyl groups in the poly(α -hydroxyacids) was shown to increase their hydrolytic degradation rates to a significant degree, because of a higher water absorption and potential autocatalytic behavior. The interest of such pendant functional groups for further chemical modification or crosslinking has also been illustrated [59].

Although the ROP of substituted 1,4-dioxane-2,5-diones allows for the preparation of ‘modified’ PLAs, its application is limited from a practical standpoint by the only moderate polymerizability of these monomers. Activated equivalents thereof would be highly desirable, and from this point of view O-carboxyanhydrides (OCAs) appear very promising candidates [60]. Indeed, the organocatalytic

7) For the related monomers **22b–24b** featuring a lactate unit, competitive cleavage of the two ester groups occurs, resulting in a statistical distribution.

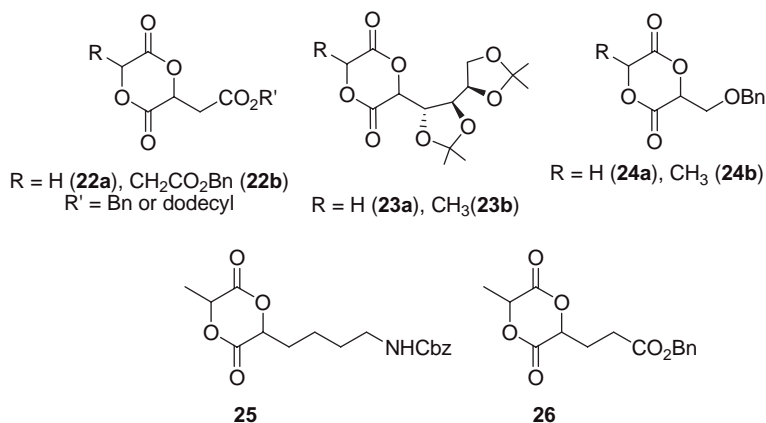
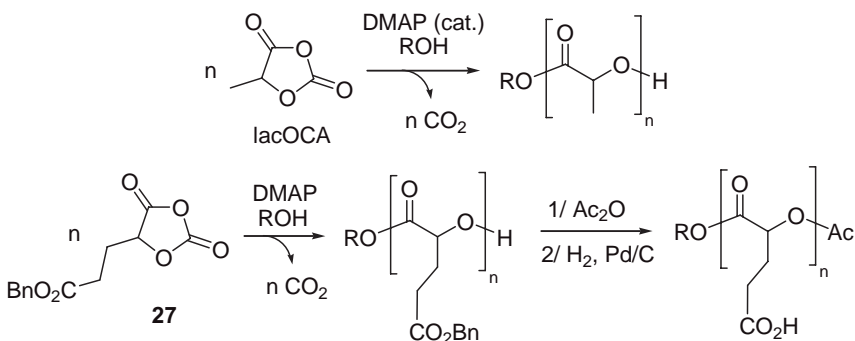


Figure 10.16 Functionalized 1,4-dioxane-2,5-diones.



Scheme 10.13 Preparation of poly(α -hydroxyacids) by ROP of O-carboxy anhydrides.

DMAP/ROH system that requires prolonged heating with lactide afforded PLAs of controlled molecular weights and narrow polydispersities, in only a few minutes at room temperature, from lacOCA (Scheme 10.13) [61]. The much higher reactivity of lacOCA, compared with lactide,⁸⁾ and the ensuing milder polymerization conditions, broaden the scope of compatible initiators so as to include functionalized ones, as illustrated with 2-bromoethanol [61a]. In addition, the high polymerizability and structural versatility of the OCAs facilitate access to modified PLAs, as exemplified by the homopolymerization of the functionalized monomer **27**. Accordingly, poly(α -hydroxyacids) derived from glutamic acid, which at one time were barely accessible from substituted 1,4-dioxane-2,5-diones, can now be prepared under mild conditions, and subsequently acetylated and deprotected [61c].

8) Model propagation reactions were computationally investigated and the polymerization of lacOCA was predicted to be about three times more thermodynamically favorable than that of lactide.

10.4.2

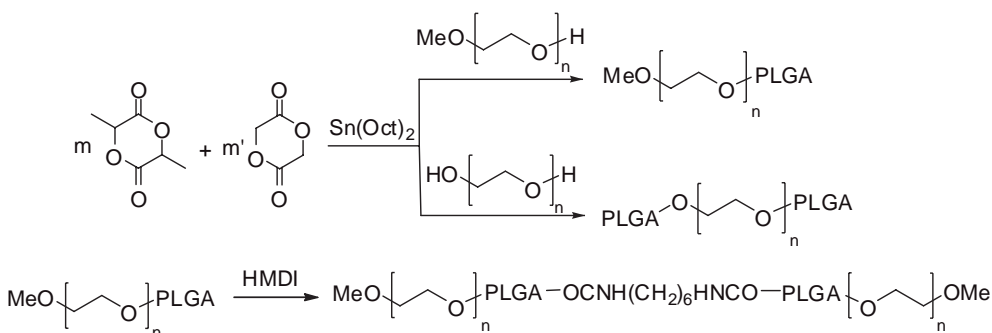
Macromolecular Architectures

Aiming at modulating further their physical and chemical properties, and thereby at extending their application fields, PLGAs have been incorporated into a broad variety of macromolecular architectures, including linear/grafted block copolymers and star/dendritic polymers.

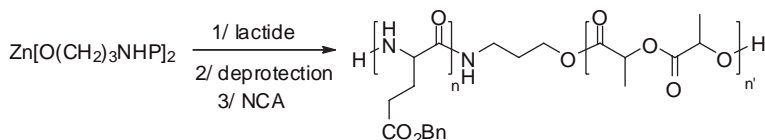
10.4.2.1 Linear Block Copolymers

Block copolymers do not suffer from the deleterious segregation effects typically associated with polymer blends. Accordingly, the properties of different polymers can be combined within a single material, and such a covalent linkage may even result in new properties. Due to their hydroxyl chain-end(s), polyethyleneglycol polymers (Me-PEG and PEG) are well-suited macroinitiators for the ROP of lactide and glycolide, giving access to Me-PEG-PLGA diblock and PLGA-PEG-PLGA triblock copolymers (Scheme 10.14). Further reaction of the Me-PEG-PLGA hydroxyl chain-end with hexamethylenediisocyanate (HMDI) leads to the *inverse* triblock copolymer Me-PEG-PLGA-PEG [62]. Due to the combination of hydrophilic (PEG) and hydrophobic (PLGA) blocks, these PLGA-PEG copolymers present amphiphilic properties, and readily form micelles in dilute aqueous solution. At a higher concentration, the aggregation of these micelles may lead to hydrogels with temperature-dependent reversible gel–sol transitions [62]. Such systems have considerable potential as sustained release matrices for active ingredients.

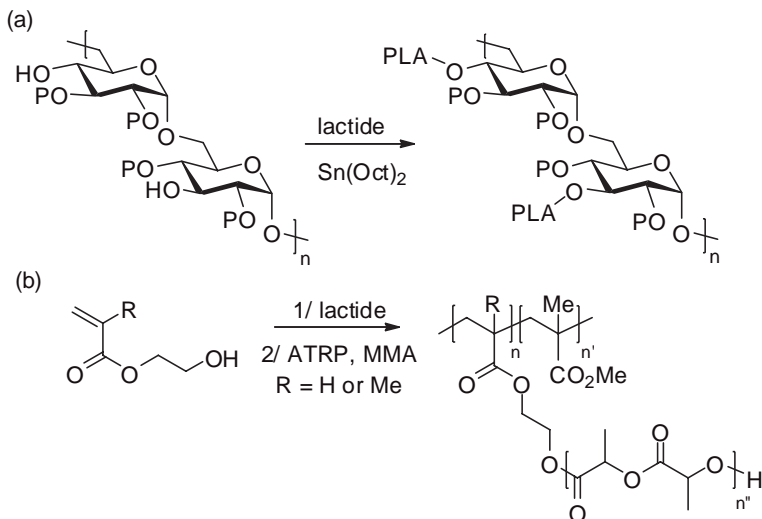
Alternatively, block polymers may be prepared by the sequential polymerization of two monomers using a bifunctional initiator, as exemplified by the preparation of diblock peptide–polylactide copolymers. *tert*-Butoxycarbonylaminopropanol is first engaged in the zinc-promoted ROP of lactide and, after deprotection of the terminal amine chain-end, the polyamide block is obtained by ROP of the *N*-carboxyanhydride (NCA) derived from γ -benzyl glutamate (Scheme 10.15) [63]. Such diblock peptide–polylactide copolymers also have interesting self-assembling properties [63].



Scheme 10.14 Preparation of diblock and triblock PLGA–PEG copolymers.



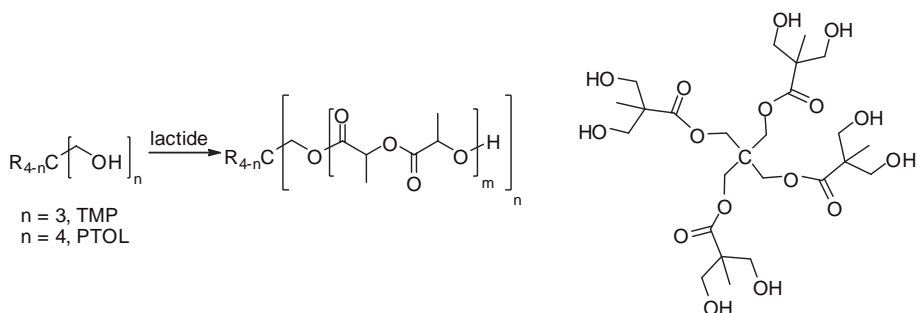
Scheme 10.15 Preparation of peptide-poly(lactide) block copolymers (P = CO₂t-Bu).



Scheme 10.16 Preparation of PLA-grafted copolymers according to (a) 'grafting from' and (b) 'grafting through' strategies. P = protective group.

10.4.2.2 Grafted Block Copolymers

Poly(lactides) have also been introduced as pendant chains in grafted block copolymers, following either the 'grafting from' or the 'grafting through' strategy. The first route consists of the growth of PLA grafts on a polymer chain featuring pendant hydroxyl groups. This strategy is commonly used for the preparation of poly(lactide)-grafted polysaccharides, as exemplified by the PLA-grafted dextran (Scheme 10.16a) [64]. After protection of the majority of the hydroxyl groups, the PLA grafts are generated by ROP of lactide initiated with Sn(Oct)₂ from the remaining hydroxyl groups. Finally, hydroxyl deprotection leads to the amphiphilic grafted copolymers with self-organization properties that show promise for applications as biocompatible surfactants. The 'grafting through' approach – which is also known as the 'macromonomer method' – has been developed particularly for PLA-grafted polyolefins (Scheme 10.16b) [65]. Typically, a (meth)acrylate-terminated poly(lactide) is first prepared by ROP of lactide initiated with 2-hydroxyethyl (meth)acrylate, and subsequently copolymerized with a low-molecular-weight monomer (such as methacrylate). Taking advantage of the recent progress made in both the ROP of lactide and atom transfer radical polymerization (ATRP) of (meth)acrylics, this strategy allows for the preparation of well-defined architectures



Scheme 10.17 Star polylactides and a representative dendritic initiator for lactide ROP.

that combine the structural properties of polymethacrylate with the biodegradability of PLAs, and are therefore promising candidates as emulsifiers, thermoplastic elastomers or impact-resistant plastics [64].

10.4.2.3 Star and Dendritic Polymers

Modifications in the polymer topology (linear \rightarrow star polymer) may also have an important influence on the polymer properties such as viscosity, degradation rate and characteristic temperatures (T_g and T_m). The ‘core-first’ strategy is more widely used than the ‘arm-first’ strategy in the case of PLAs. Accordingly, a multifunctional core, such as trimethylolpropane (TMP) or pentaerythritol (PTOL), is typically used as an initiator for the $\text{Sn}(\text{Oct})_2$ -promoted ROP of lactide (Scheme 10.17) [66]. Even more complex topologies are available using dendritic structures featuring functional groups active as ROP initiators on their surfaces. For this purpose, dendrimers derived from 2,2’-(bishydroxymethyl)propionic acid have been successfully applied (Scheme 10.17) [67]. Nitrogen-based dendrimers have also been used as initiators [68].

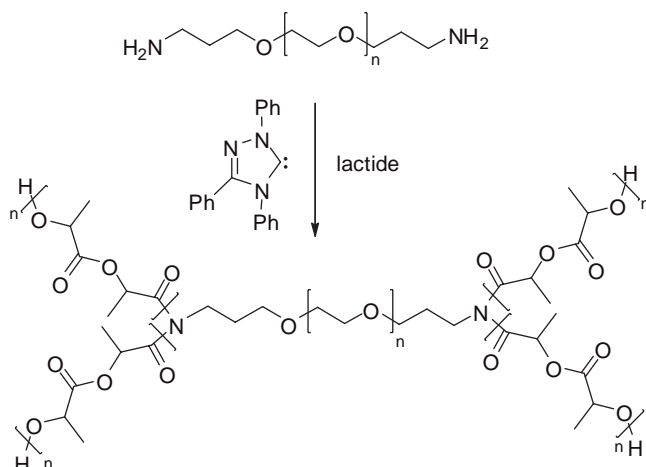
Recent advances in the metal-free ROP of lactide also contribute to the development of new macromolecular architectures, as illustrated by the preparation of H-shaped copolymers from the ROP of lactide initiated with $\text{PEG}-(\text{NH}_2)_2$ and catalyzed by a triazolydene (Scheme 10.18) [69].

10.5

Applications

As mentioned previously, PLAs and related copolymers are biodegradable and bioassimilable, while their properties can be tuned by varying their structural parameters. All of these aspects have given rise to a broad range of medical (surgical and pharmaceutical) and commodity applications (packaging, fibers) [3e–k].

The first medical applications date from the 1970s, and the spectacular technological advances achieved over the past 40 years have allowed further developments, including highly sophisticated devices [3i]. In particular, significant progress has been reported in surgery with resorbable sutures, orthopedic devices, stents and, more recently, tissue engineering. With these devices, no particular



Scheme 10.18 An H-shaped PLA-PEG copolymer.

precautions are necessary for their use and there is no need for a removal operation, which is highly advantageous compared with metal analogues. Dexon (a multifilament PGA material) and Vicryl (a PLGA copolymer containing 8% lactic acid and 92% glycolic acid) were the first sutures based on PLGA polymers [70]. The variety of resorbable sutures has subsequently been extended by combining PLGAs with other biodegradable polyesters, for example poly(ϵ -caprolactone) (PCL) or polycarbonates (e.g. poly(trimethylene carbonate) [2i]. Mechanical properties exhibited by PLGAs, such as high modulus and tensile strength, and low elongation at break, make them also suitable for orthopedic fixations, and even as bone-substitution materials. The ligating clips and bone pins produced from Lactomer (a PLGA copolymer containing 70% lactic acid and 30% glycolic acid) are representative examples of such orthopedic devices that are commonly used [71]. A potential drawback of these devices is the inflammation that may appear in the vicinity of such implants; this is often attributed to the acidity induced by the release of monomeric or oligomeric carboxylic acids upon degradation [72]. To overcome this problem, the use of basic inorganic additives (calcium phosphates, carbonates or hydrogenocarbonates and hydroxyapatites) is under investigation [73].

Besides these developments in surgery-related applications, numerous examples have been reported in pharmacology using drug-loaded, biodegradable devices. These formulations improve the therapeutic efficiency and increase patient compliance by decreasing the administration frequency and adverse side effects [74]. A wide variety of active ingredients, from low-molecular-weight steroids to high-molecular-weight polypeptides (including human growth hormone) have been formulated in this way to target a variety of pathologies. These drug-delivery systems are often formulated as implants or microparticles which are administered subcutaneously. For example, Lupron Depot, a one-month injectable formulation based on microspheres of PLGA and leuporelin acetate, is widely used in the treatment of endometriosis and prostate cancer [75]. Forthcoming progress in this area will extend this approach to oral [76], nasal [77] and intravenous administrations. The

problems associated with the rapid uptake of intravenously injected particles by the cells of the reticuloendothelial system may be circumvented by using small-size particles (typically < 100 nm) and amphiphilic copolymers derived from PLGAs [78]. Efforts have also been devoted to the elaboration of more sophisticated drug-delivery systems. For example, a resorbable polymeric microchip device allowing the multipulse delivery of several active ingredients without external stimulation deserves mention here as a promising achievement [1, 79].

Poly(α -hydroxy-acids) offer a practical solution to the ecological problems associated with petrochemical-based plastics and the ensuing bioresistant wastes. Indeed, PLAs not only exhibit appropriate physical and mechanical properties [1, 2j] but are also biodegradable and available from 100% renewable resources, as a result of the Natureworks process [1]. The tensile strength values of high-molecular-weight PLAs are within the same range as those of polystyrene (PS), and slightly lower than those of poly(ethylene terephthalate) (PET). These have excellent grease resistance, and good barrier properties to flavors and ultraviolet light. In addition, their rheological properties make them suitable for sheet extrusion, injection molding, film blowing and thermoforming. These properties, combined with a low temperature heat sealability and good crease retention, have been exploited in the manufacture of food packaging, such as flexible films, rigid containers, drink cups and bottles [1, 2k].

Finally, the fiber spinning of polymers derived from lactic acid has also given rise to PLA-based fibers, registered as Ingeo fibers. Pillow liners and duvets made from this material are already available, and clothing applications are rapidly developing, with PLAs providing the same wearing comfort as PET or cotton, but with better dimension stability [1, 2k].

10.6

Summary and Prospects

Synthetic polyesters resulting from the ROP of dilactones (especially lactide and glycolide) have attracted considerable interest from both academic and industrial viewpoints. Spectacular progress has been made in terms of activity and polymerization control with both single-site metal complexes and organocatalysts. The stereocontrolled ROP of lactide has also developed considerably with, in particular, efficient systems having been reported for the preparation of high-melting stereocomplexes from *rac*-lactide, while a better understanding of the factors that precisely govern chain-end and site stereocontrol will lead to further progress. In order to modulate the physical and chemical properties of PLAs, alternative functionalized and activated monomers have been evaluated in ROP. The formation of various macromolecular architectures such as block, star and dendritic (co)polymers has further extended the range of available material properties. All of these developments have contributed to the increasing use of PLAs in medical and commodity applications, and the Natureworks production of PLAs from 100% renewable resources is likely to accelerate further these developments.

Acknowledgments

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11

Polyesters from Large Lactones

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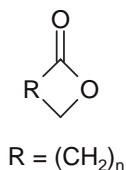
11.1

Introduction

Aliphatic polyesters prepared by the ring-opening polymerization (ROP) of lactones and lactides are versatile polymers with good mechanical properties, hydrolyzability, biodegradability and biocompatibility. These attributes make them a leading candidate in the biomedical and pharmaceutical industries. These polyesters have been considered for a variety of medical applications (e.g. as prosthetics, artificial skin, etc.) and in pharmaceutical industries for drug-delivery applications. Polylactides (PLAs) have been used for the long-term delivery of antimalarial drugs, contraceptives and as formulation to treat eye conditions. The biomedical applications of these polymers have been reviewed recently [1]. Poly(ϵ -caprolactone) (PCL) has received much interest in applications such as mulch films, ropes or cups utilizing its biodegradability, and permeability in agricultural areas or in composting facilities [2]. Today, several aliphatic polyesters such as poly(lactic acid) and PCL are produced commercially in large volumes for applications as a packaging materials and commodity plastics.

Studies of the ROP of cyclic esters have primarily focused on the small (glycolide, lactide, γ -butyrolactone, δ -valerolactone, etc.) and medium-sized (ϵ -caprolactone (CL), 1,5-dioxepan-2-one (DXO), etc.) rings, which have angular or transannular strains [3–10]. A ‘large ring’ on the other hand, is defined as a ring containing 12 or more atoms; there is no upper limit to this number, although very few reports are available on lactones with more than 16 atoms. These large-ring lactones or macrolides possess diverse biological and medicinal properties, and are used, for example, as musk deodorants. Unlike the small and medium-sized rings, which are considerably strained, these large rings are relatively strain free (some examples are shown in Scheme 11.1). They can be prepared in moderate to good yields by using a variety of direct cyclization procedures of hydroxy carboxylic acid, or other methods [11].

A general procedure for the synthesis of polyesters is provided in Scheme 11.2.



$n = 1$; β -Propiolactone (PL)

$n = 6$; 8-Octanolide (OL)

$n = 2$; γ -Butyrolactone (γ -BL)

$n = 9$; 11-Undecanolide (UDL)

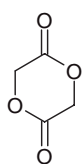
$n = 3$; δ -Valerolactone (VL)

$n = 10$; 12-Dodecanolide (DDL)

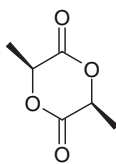
$n = 4$; ϵ -Caprolactone (CL)

$n = 13$; 15-Pentadecanolide (PDL)

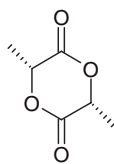
$n = 14$; 16-Hexadecanolide (HDL)



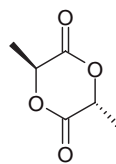
Glycolide



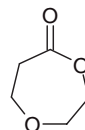
L-lactide



D-lactide

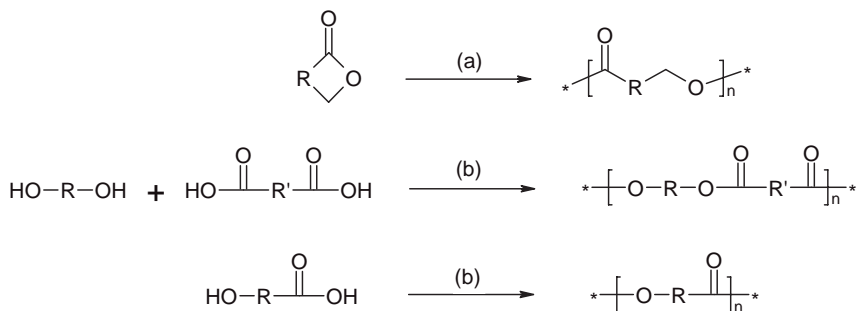


D,L-lactide



1,5-Dioxepan-2-one

Scheme 11.1 Lactones/lactides of different ring size.



Scheme 11.2 Synthetic routes for the preparation of polyesters. (a) Ring-opening polymerization; (b) polycondensation.

In this chapter we will discuss the ROP and copolymerization of medium-ring sized (i.e. 7- to 11-membered) and large ring lactones (12- to 17-membered), using nonenzymatic (anionic, cationic and organometallic initiators) as well as enzymatic methods. The preparation of polyesters with pendant functionality or end-functionality will also be described, and the physical properties and potential applications of such polyesters briefly mentioned.

11.2

Controlled Synthesis of Linear Polyesters

The ROP method of converting lactones into well-defined, high-molecular-weight polyesters has been extensively investigated and refined during the past few decades. Several efficient catalysts have been developed for the preparation of these polyesters, with alkaline and multivalent metal aliphatic alkoxides, alkylalkoxides, acyloxides, carboxylates, acetylacetonates [2], protonic acids, carbenes [12] or enzymes all having been investigated for the ROP of lactones. In some of these initiating systems, the presence of water, aliphatic alcohol or primary amine is required to start the polymer chain. Previously, two major ROP mechanisms have been proposed: (i) the activated monomer mechanism; and (ii) the coordination–insertion mechanism. Both mechanisms are believed to be initiated by alcohol, and most often the degree of polymerization is dependent on the monomer/alcohol ratio, leading to end-groups of polyester chains that are end-capped by hydroxyl group(s). During the past few years, a number of reviews have been presented describing with the synthesis of polyesters by the ROP of lactones [1, 2, 13–19].

Unfortunately, in the polymerization of macrolides or large-ring lactones, most of the above-mentioned methods yield only oligomers or low-molecular-mass polymers. Attempts have been made to correlate the ring-opening polymerizability of lactones with factors such as ring-strain, hydrolysis rate or their basicity. The thermodynamic data for small and medium-sized lactones show that the entropy change during polymerization is negative; thus, the driving force for the polymerization of these lactones is the negative change of enthalpy. The ROP of highly strained three- and four-membered ring lactones is a favorable reaction, the driving force being the release of angular strain (Bayer's strain). The presence of substituents at the ring carbons may further increase the strain, and thus increase the exothermicity of the reaction. In medium-sized rings, such as seven-membered lactones, the relief of intramolecular crowding (transannular strain) is the driving force. The ΔG_p^0 values for β -propiolactone, γ -butyrolactone, D,L-lactide, 1,4-dioxan-2-one and CL have been reported as -82.3 , $+5.1$, -22.9 , -13.8 and $-28.8 \text{ kJ mol}^{-1}$, respectively [20]. The ΔG_p^0 is positive for γ -butyrolactone, indicating that the ROP of γ -lactone is thermodynamically unfavorable [21, 22]; however, by employing drastic reaction conditions the (co)polymerization may be carried out.

The polymerizability of macrolides is expected to be much lower than that of CL or DXO because of the strain-free character of the large-sized rings. Only a few studies have been reported on polyesters derived from macrolactones by non-methods, although in some of these no detailed description of the polymerization method has been provided. Skoglund and Fransson, for example, reported the thermophysical properties of polytridecanolactone and polypentadecanolactone, but failed to describe their method of preparation [23, 24].

11.2.1

Nonenzymatic Methods of Polymerization

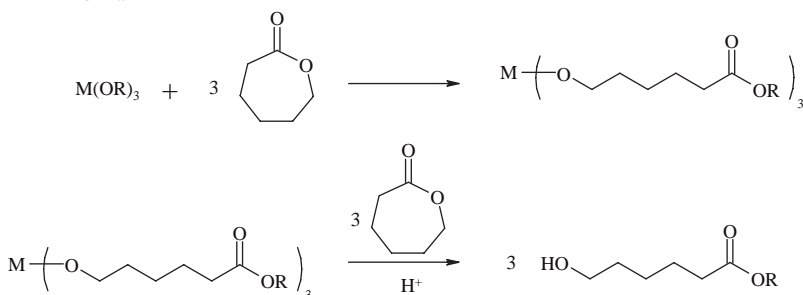
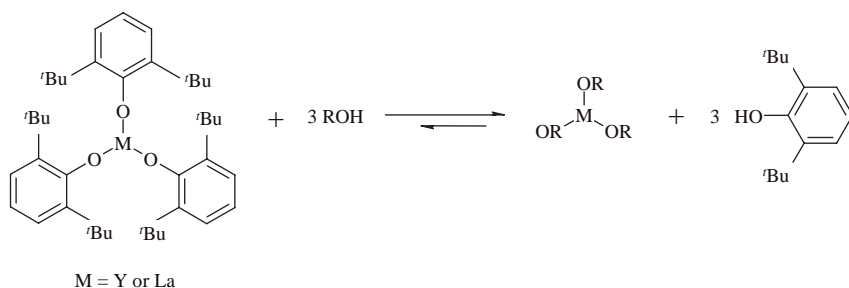
The most effective initiators for anionic polymerization are alkali metals, alkali metal oxides (lithium, sodium and potassium alkoxides) and alkali metal naphthalenide complexes with crown ethers [2]. Anionic polymerizations are sometimes associated with termination and transfer reactions, while cyclic oligomers are formed as a result of back-biting reactions. In CL polymerization initiated with potassium *tert*-butoxide, a huge amount of cyclic lactones was formed, yet in the presence of lithium *tert*-butoxide in an apolar solvent the oligomer formation was significantly reduced.

The polymerization of 12- and 13-membered lactones has also been reported by using anionic initiators [25]. The polymerization was carried out in bulk or in solution [using tetrahydrofuran (THF) as solvent] with metal (Li, Na or K) methoxide as anionic initiators under a nitrogen atmosphere. The optimum temperature for the polymerization in bulk was found to be 120 °C. The polymers were obtained in good yields, with the number average molecular mass (M_n) obtained with 13-membered lactone (oxycyclotridecan-2-one or dodecanolide) at 120 °C being 11 000 g mol⁻¹, and with 12-membered lactone (oxycyclododecan-2-one or undecanolide) 8900 g mol⁻¹. The counterions had a negligible effect on the yields or molecular mass of the polymers. Other anionic initiators, such as butyl lithium or diethyl zinc, proved to be ineffective for the polymerization of these lactones. In solution polymerization, small amounts of cyclic oligomers and linear oligomers were also formed due to back-biting reactions. The propagation rate constants for the macrocyclic esters were found to increase with an increase in s-character of the methylene carbon [25].

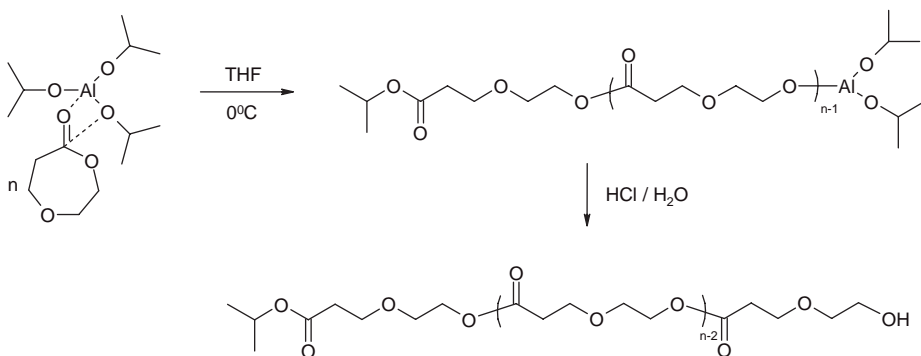
The anionic polymerization of 16-membered-lactone, ω -pentadecalactone (PDL), initiated with potassium alkoxide under mild conditions was reported by Jedlinski *et al.* [26]. These authors showed that polymerization would occur under mild conditions (THF, 35 °C) to form high-molecular-mass polymers (M_n up to 100 000 g mol⁻¹), although the formation of cyclic oligomers via a back-biting reaction was also noted.

Lanthanide compounds such as yttrium and lanthanum alkoxides have been reported to yield high-molecular-mass polyesters under mild conditions. The yttrium alkoxide-initiated polymerization of CL proceeded rapidly at room temperature [27–29], while the use of bulky groups reduced the transesterification reaction such that polymers with a narrow molecular mass were obtained (Scheme 11.3). For example, the bulky phenoxide ligands of the yttrium or lanthanide catalyst were exchanged for the smaller alcohol (2-propanol), followed by coordination and insertion of the monomer (CL) [27].

The aluminum alkoxide-initiated polymerization of lactones such as CL and DXO proceeds by a coordination–insertion mechanism, which involves acyl–oxygen bond cleavage of the monomer and insertion into the aluminum–oxygen bond of the initiator. The coordination of the exocyclic oxygen to the metal results in polarization, which in turn makes the carbonyl carbon of the monomer more



Scheme 11.3 Reaction sequence for the synthesis of narrow molecular mass PCL [27].

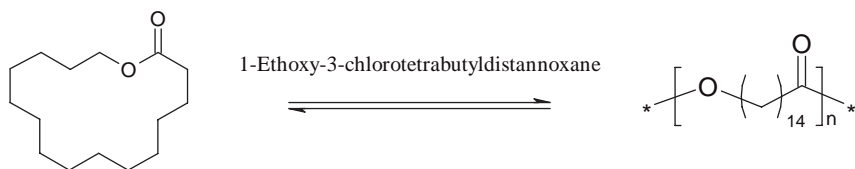


Scheme 11.4 Polymerization of DXO using aluminum-isopropoxide.

susceptible to nucleophilic attack (see also Chapter 10). Transesterification may also take place at elevated temperatures. A poly(DXO) of $M_n = 17\,500 \text{ g mol}^{-1}$ could be prepared by polymerization at 0°C [30] (Scheme 11.4).

The 'living' ROP of CL is usually initiated by aluminum isopropoxide in toluene at 0 – 25°C . The initiation rate is high compared to the rate of propagation, so that a narrow molecular weight distribution [M_w/M_n , polydispersity index (PDI)] is obtained. There is no termination reaction and three polymer chains grow for each Al atom [30]. A–B diblock copolymers of oxepan-2,7-dione and 2-oxepanone have been prepared by using this method [31].

Carboxylates are less nucleophilic than alkoxides, and are considered to behave more like a catalyst than an initiator [2]. Tin(II) 2-ethylhexanoate [$\text{Sn}(\text{Oct})_2$] is used together with active hydrogen compounds such as alcohols as initiators [32, 33].



Scheme 11.5 Polymerization scheme of pentadecalactone with distannoxane catalyst.

Albertsson *et al.* have conducted extensive studies on the homo- and copolymerizations of lactones in bulk (100–150 °C) and in solution (0–25 °C) [34–37], and poly(DXO) of high molecular mass was obtained by using $\text{Sn}(\text{Oct})_2$ [34]. The reactivity ratios in the random copolymerization of DXO and CL have been reported as $r_{\text{DXO}} = 1.6$ and $r_{\text{CL}} = 0.6$.

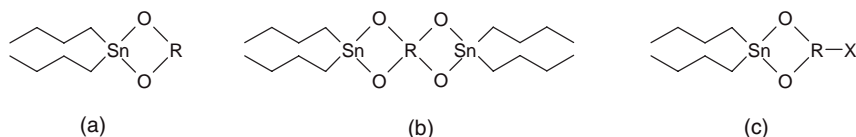
Hori *et al.* reported the copolymerization of a 16-membered dilactone, ethylene dodecanedioate, catalyzed by a distannoxane complex [38]. The polymer was obtained in good yield (97%) after having carried out the bulk polymerization for 96 h at 95 °C, and had a M_n of 148 000 g mol^{-1} and a PDI of 1.59 (Scheme 11.5).

The polymerization of PDL, initiated by yttrium isopropoxide, has been carried both in bulk and in solution over the temperature range of 60–100 °C [39]. All isopropoxide groups of the initiator participated in the initiation, and the polymerization proceeded by acyl–oxygen cleavage of the monomer. The molecular mass of the polymer could be controlled effectively by varying the initial monomer-to-initiator molar ratio. An induction period which was observed for the bulk polymerization at 60 °C was attributed to structural rearrangement processes of the initiator to form the actual active sites. The molecular weight distribution (PDI) was approximately 1.6.

The polymerization of PDL by using aluminum triflate (trifluoromethane sulfonate) has been reported recently [40]. Using glycerol as an initiator, the bulk polymerization was carried out at 100 °C for 6 h to produce a polymer (yield 49%) of M_n 12 400 g mol^{-1} and PDI 2.24.

The kinetics of ROP of various ring-sized lactones (e.g. 12-, 13-, 16- and 17-membered) initiated by zinc-2-ethylhexanoate/butyl alcohol system at 100 °C was investigated by Duda *et al.* [41]. The relative rates of polymerization were almost comparable, and seemed to be independent of the ring size variation from 12 to 17 atoms; however the polymer formed had very low M_n values (1350–1700 g mol^{-1}). In the absence of any available data on the thermodynamic polymerizability of larger lactones (i.e. enthalpy and entropy values), these authors have supplemented the same by comparing the dipole moments of different ring-size lactones as a measure of ring strain. The dipole moments of medium-sized lactones (six- or seven-membered) were significantly higher, whereas those of the 12-, 13- and 16-membered rings were comparable to that of an aliphatic ester (butyl caproate). Based on these data, it was concluded that the polymerization of large-ring is essentially driven by a positive change in entropy.

Linear, cyclic and spirocyclic structures with functional groups such as hydroxyl, carboxyl or amino have been prepared using $\text{Sn}(\text{IV})$ alkoxides, such as tributyl tin alkoxide and dibutyl tin alkoxide. Some of these structures are depicted in Scheme 11.6. Dibutyl tin alkoxide dissolved in tetrabutyl tin is believed



Scheme 11.6 Tin(IV) initiators. (a) Cyclic; (b) spirocyclic; (c) functionalized.

to be the main initiator for the polymerization of CL [42], while tributyl tin methoxide and dibutyl tin dimethoxide have been used for the bulk polymerization of lactones and lactides [43, 44]. A coordination–insertion mechanism has been suggested for the ROP of DXO using Sn(IV) alkoxide [45]. Some details of studies on cyclic tin initiators have also been reported [46–50]; for example, when Kricheldorf *et al.* [47] described for the first time spirocyclic Sn(IV) alkoxides for the ROP of CL, a high-molecular-mass PCL with a PDI of less than 2 was obtained using this initiator.

11.2.2

Enzymatic Methods of Polymerization

In vitro enzyme-catalyzed ROP in a nonaqueous medium has been extensively investigated during the past 15 years (see also Chapter 15). The benefits of using enzymes as catalysts instead of nonenzymatic methods include:

- only mild reaction conditions are required
- the enzymes are recyclable, ecofriendly and nontoxic materials. Their removal from the polymers is not stringent, whereas in nonenzymatic processes the removal of nondesirable chemical residues from the polymer is essential
- enzymes provide synthetic routes to complex structures
- macrolides that cannot be polymerized to high-molecular-mass polymers by nonenzymatic methods are recognized by the enzymes, and this leads to the formation of high-molecular-mass polymers.

The lipase-catalyzed ROP of small-, medium- and large-ring lactones has often been reported. By definition, lipases hydrolyze triglycerides in an aqueous medium at one or more of the three ester bonds, and have been characterized by their drastically increased activity at the lipid–water interface of a micellar or emulsified substrate. In a nonpolar medium, these enzymes are capable of initiating the ROP of cyclic lactones, and this property has been exploited for the synthesis of polyesters, especially from macrolides.

Most such carboxylic ester hydrolases (lipases) contain a Ser-His-Aspartate/Glutamate catalytic triad (Ser105–His224–Asp187) in the active site, and share (at least in part) the common structural framework of the α,β -hydrolase fold. This fold is composed mainly of parallel β -sheet, flanked on both sides by α -helices [51]. A unique structural feature common to all lipases is a ‘lid’ or ‘flap’ composed of an amphiphilic α -helix peptide sequence which, in its closed conformation, prevents access of the substrate to the catalytic site [52]. When the lid is opened,

a large hydrophobic surface is created to which the hydrophobic substrate can bind.

The polymerization behavior of macrolides was found to depend on the origin of the lipase, the size of the ring, position of the substituent, the type of organic solvent, the water content, and the temperature of polymerization. Several macrolides ranging from 12- to 17-membered rings have been polymerized using lipase catalysis. One especially attractive property of lipases is their ability to react selectively with one of two enantiomers of secondary alcohols, and in this respect they serve as efficient stereoselective catalysts in the kinetic resolution of a wide variety of chiral compounds. In this situation, the fast-reacting enantiomer could bind to the enzyme with an intact hydrogen bond between the alcohol oxygen and the NH group of the active-site histidine. Such a bond is not formed with the slow-reacting enantiomer.

Water is critical for enzymes because it influences enzyme structure via noncovalent bonding. A too-low water content generally reduces enzymic activity, whereas a too-high content can also reduce the reaction rates by causing the aggregation of enzyme particles and hence diffusional limitations. The optimum water content is often within a narrow range.

Those lipases that have been reported for the polyester synthesis are of mammalian (porcine pancreatic lipase, PPL) or fungal (*Candida antarctica*, CA; *Candida rugosa*, CR; *Candida cylindracea*, CC; *Aspergillus niger*, AN; *Penicillium roureforti*, PR; *Rhizopus delemar*, RD; *Rhizomucor miehei*, RM) or bacterial origin (*Pseudomonas cepacia*, PC; *Pseudomonas fluorescens*, PF; *Pseudomonas species lipase*, PS) and so on.

Uyama *et al.* [53–55] were the first to report details of the lipase-catalyzed polymerization of macrolides such as 11-undecanolide (UDL), 12-dodecanolide (DDL) and 15-pentadecanolide (PDL). The polymerization was initiated by using lipases of different origin; those of the *Pseudomonas* family were found to be the most active, and yielded at 75 °C a poly(UDL) with a high monomer conversion (>90%) and M_n of 10^4 g mol^{-1} . The polymerization rate of UDL in comparison to ϵ -caprolactone was higher with the lipase from *Pseudomonas fluorescens*, an effect which has been attributed to the strong recognition of macrolides by lipase. The polymerization of PDL using *Pseudomonas fluorescens* and *Pseudomonas cepacia* below 45 °C was low, although increasing the temperature to 60 °C or above caused an increase in the polymerization rate. *Candida cylindracea* yielded a polymer of high molecular mass only above 75 °C.

The polymerization of DDL also increased significantly depending on the origin of the lipase. For example, the highest rate was observed with lipase PC, followed by PF, CC and PPL. The molecular mass was also increased in line with an increase in temperature, from 30 to 75 °C [55].

Bisht *et al.* also reported the polymerization of PDL using a lipase of different origin. Lipozyme IM, PS-30 and Novozyme 435 each gave higher conversions (80–100%) for a 24 h reaction at 80 °C [56], with the M_n being in the range of 15 000 to 34 400 g mol^{-1} . Higher reaction rates were observed when immobilized enzymes were used. Water was an important factor in controlling the rate of polymerization

and molecular mass of the polymer. At low water levels (0.2%, w/w), a polymer with M_n 62 000 g mol⁻¹ and PDI of 1.9 was obtained; however, an increase in temperature from 60 to 80 °C resulted in increases not only in the rate but also the molecular mass of the polymer.

The effect of water content on the ROP of UDL and PDL was also investigated by Matsumoto *et al.* [57], who suggested that in the initiation step, the lactone reacted with water through the acyl-enzyme to yield the hydroxyl acid. In the propagation step, the lactone would then react with the hydroxyl group or polymer through the acyl-enzyme complex. Noda *et al.* [58] noted a higher rate of polymerization and M_n by using surfactant-coated lipase PS.

Duda *et al.* [41] have investigated the kinetics of ROP of lactones of different ring sizes by using a nonenzymatic (zinc-2-ethylhexanoate/butyl alcohol) system at 100 °C, and compared the results to those with enzymatic methods. The decreasing order of rates for nonenzymatic methods showed a reverse trend to that of enzymatic polymerization. The 17-membered lactone was most reactive towards enzymatic polymerization, a fact attributed to thermodynamic factors in chemical polymerization, while the hydrophobicity of the large-ring lactones was seen as the major contributory factor for enzymatic polymerization. The introduction of an α -methyl substituent reduced the polymerizability of 13- and 16-membered lactones, and a reduction in monomer conversion as well as M_n was observed [59].

A significant difference in the rate of Novozyme 435-catalyzed polymerizations of lactones of different ring sizes (6-, 13- and 16-) has been reported recently. The initial rate constants for 10-decalactone, UDL and DDL were 0.10, 0.38 and 4.9 h⁻¹, respectively, but these differences could not be correlated with physical properties such as dipole moments, which are approximately 1.9 D in all these monomers. When the Michaelis-Menten constants K_m and V_{max} were measured [60], the K_m was shown to be independent of the ring size, which suggested similar affinities of the lipase for all the lactones; however, no obvious trend was observed in V_{max} values. Namekawa *et al.* [61] have discussed the mechanistic aspects of lipase-catalyzed ROP of polyesters, while Kobayashi *et al.* [62] have reported the polymerization of UDL, DDL and PDL by lipase PC and PF in aqueous media. However, the polymers formed had a low molecular mass of 1×10^3 g mol⁻¹.

A high-molecular-weight poly(DXO) was obtained via lipase CA-catalyzed polymerization at 60 °C, using an optimum amount of water as an initiator. An increase in the temperature of polymerization from 60 to 80 °C resulted in an increased polymerization rate and degree of polymerization (DP) of the polymer chains. However, a further increase in temperature reduced the rate of polymerization, most likely due to denaturation of the enzyme [8].

Stable miniemulsions in water, consisting of PDL droplets (prepared by using a nonionic surfactant and ultrasonication), could be polymerized by lipase PS to yield high-molecular-mass polyester biodegradable nanoparticles [63].

Seven-membered lactones such as DXO and CL showed different reactivity in lipase CA-catalyzed polymerization initiated by different alcohols [7]. The higher reactivity of DXO in these polymerizations may be attributed to the presence of

an ether linkage, which may form hydrogen bonding with the histidine NH of the catalytic triad of the enzyme.

11.2.2.1 The Mechanism of Enzyme-Catalyzed ROP

The mechanism of enzyme-catalyzed ROP was first proposed by Uyama *et al.* [54]. Here, the catalytic site of lipase is the serine residue, which forms a complex with the lactone, leading to the formation of an enzyme–monomer complex (EMC). The rate-determining step in the overall polymerization was believed to be the formation of EMC (also known as an ‘enzyme-activated monomer’).

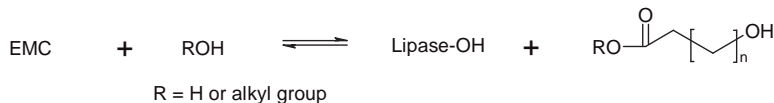
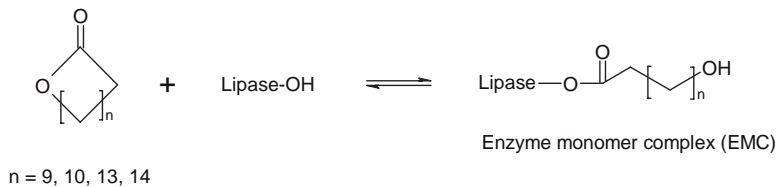
The initiation step is a nucleophilic attack of water or alcohol onto the acyl carbon of the intermediate to form a ω -hydroxyl carboxylic acid, although other nucleophiles, such as amines, may also participate in this reaction. Water is generally associated with the enzyme, or may be added to the organic solvent (Scheme 11.7).

In the propagation step, the nucleophilic attack of the terminal hydroxyl group of the ω -hydroxyl carboxylic acid on EMC leads to the formation of a one unit more-elongated polymer chain.

In contrast to this proposal, MacDonald *et al.* [64] suggested that the chain propagation of polymerization was a slow step, while Gross *et al.* [65] found that the monomer conversion followed first-order law and was independent of both the type (water, butanol and butyl amine) and concentration of the nucleophile. Yet another group suggested a complex mechanism of polymerization involving ring-opening and linear condensation polymerization [66].

The main feature of enzyme catalysis involves the formation of an acyl–enzyme intermediate as a key step, although whether this step or the subsequent propagation step is rate-determining remains the subject of controversy. Recently, Kobayashi [17] suggested that the acylation step (formation of the acyl–enzyme intermediate) and/or a nucleophilic attack of the propagating alcohol end to the

Initiation



Propagation



Scheme 11.7 Postulated mechanism of lipase-catalyzed polymerization of lactones.

carbonyl carbon of the intermediate to open the monomer ring (deacetylation step), might each be rate-determining. The structure of the propagating alcohol end (primary or secondary) determines which step is rate-determining, whereas the deacetylation step only becomes rate-determining when the propagating alcohol end is capable of steric hindrance. It is possible, therefore, that enantioselection may be induced at both the acetylation and deacetylation steps.

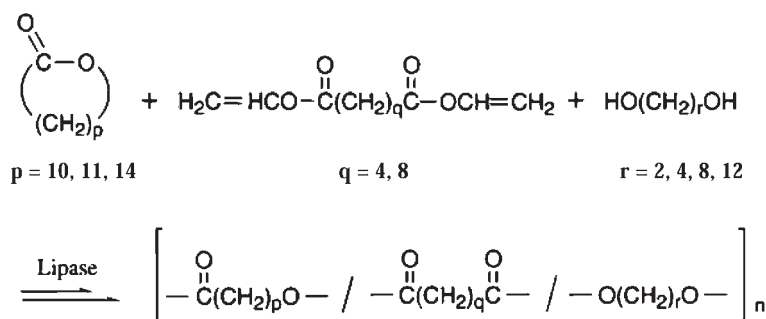
11.2.3

Copolyesters

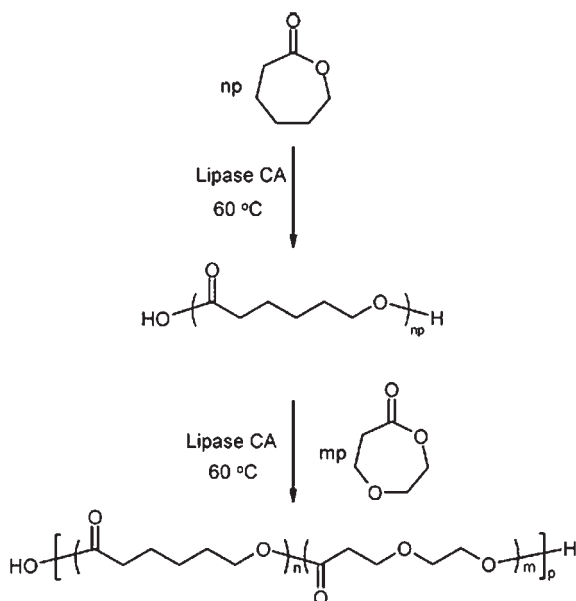
The copolymerization of 12-, 13- and 16-membered lactones, divinyl esters of adipic and sebacic acid and α,ω -glycols by using *Candida antartica* and *Pseudomonas cepacia* lipases yielded copolymers of high molecular weight, in moderate yields (Scheme 11.8). Taken together, these results indicated that ROP and polycondensation can occur simultaneously in a one-pot reaction to yield copolyesters [67].

Copolyesters with molecular weights of several thousands could be produced by polymerizing macrolides in the presence of aliphatic polyesters. Random copolyesters containing both units were obtained, showing that the lipase had catalyzed not only the polymerization of macrolide but also the intermolecular transesterification reaction of the starting and resulting polyesters [68]. Random copolyesters were also obtained by the copolymerization of 8-octanolide with DDL [69]. Highly crystalline random copolyesters of PDL and CL have been prepared via a Novozyme 435-catalyzed copolymerization at 70 °C in toluene [70].

The enzyme-catalyzed synthesis of diblock polyesters has been reported by Kumar *et al.* [71]. Here, monohydroxyl-terminated polybutadiene with M_n of 2.6, 10 and 19 kg mol⁻¹ were capable of initiating the polymerization of PDL in the presence of CA lipase, using toluene as a solvent at 55 °C. Triblock copolyesters were prepared by using poly(caprolactone) diol or poly(ethylene glycol) as initiator for the enzyme-catalyzed ROP of CL or DXO. In these polymerizations the macroinitiator formed the middle block [7]. The lipase CA-catalyzed sequential copolymerization of CL and DXO yielded microblock copolyesters as a result of a transesterification reaction [4] (Scheme 11.9).



Scheme 11.8 Copolymerization of lactone(s), diacid(s) and diol(s) using lipase-catalyzed ROP and polycondensation.



Scheme 11.9 Sequential copolymerization of CL and DXO in lipase CA-catalyzed ROP.

Resorbable microblock copolymers based on DXO and CL and elastomeric hydrolyzable porous scaffolds based on copolymers of DXO, L-lactide and CL have recently been reported [72, 73].

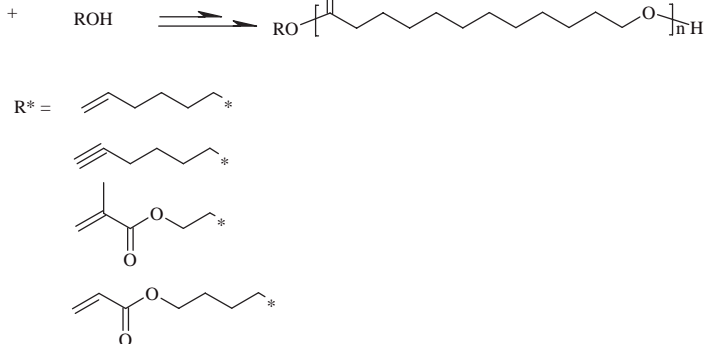
11.2.4

Functionalized Polyesters

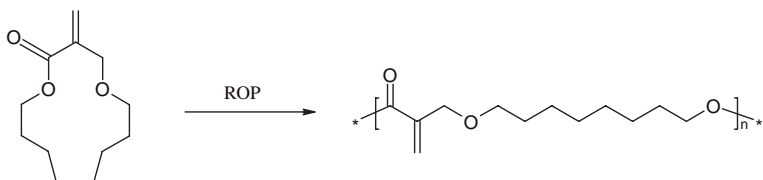
Functional polyesters are of interest for a variety of industrial and biomedical applications, as such functional groups may be utilized for the preparation of comb, graft and network polymers. Alcohols have been used to initiate the ROP of lactones to introduce the alcohol moiety at the polymer terminal. ω -Unsaturated macromonomers were synthesized by using 5-hexen-1-ol or 5-hexyn-1-ol as the initiator for DDL using lipase CA as catalyst [74]. In the polymerization of DDL, employing 2-hydroxyethyl methacrylate as initiator, the methacryloyl group was quantitatively introduced at the polymer terminal to produce the methacryloyl-type macromonomer (Scheme 11.10).

Macromonomers bearing unsaturation at the chain-end were recently reported via the ROP of CL and DXO at 60 °C, under anhydrous conditions, using 2-hydroxyethyl methacrylate (HEMA) as an initiator. The DP of the macromonomers was controlled by regulating the monomer-to-HEMA ratio, after which the macromonomers were homopolymerized or copolymerized with methyl methacrylate by free radical initiators [6].

Recent developments in the chemical synthesis of novel aliphatic polyesters via the ROP of functional cyclic diesters and esters using Al- or Sn-based initiators



Scheme 11.10 Synthesis of ω -functionalized poly(DDL).



Scheme 11.11 Chemospecific polymerization of 2-methylene-4-oxa-12-dodecanolide.

have been reviewed by Jerome and coworkers [75]. Functional aluminum alkoxides have been used to initiate the ROP of CL and lactides to produce end-functionalized chains, such that PCL with protected hydroxyl, carboxyl and amino groups have each been synthesized. Several routes for the synthesis of P(CL-g-MMA) with grafts of controlled molecular mass and polydispersity have also been reported. Aliphatic polyesters derived from CL having terminal or pendant unsaturated groups are important because these groups can subsequently be utilized for crosslinking, epoxidation, bromination, and so on [75].

11.2.5

Chemospecific Polymerization

Methylene macrolides having 12- to 17-membered rings and various functional groups have been polymerized chemospecifically to afford polyesters via enzymatic ROP, thus keeping the methylene double bonds intact. For example, the chemospecific polymerization of 2-methylene-4-oxa-12-dodecanolide yields polyesters by ROP catalyzed by lipase CA [76, 77] (Scheme 11.11). The polyesters thus obtained had a highly reactive methylene group in the repeating unit, which may be utilized for further polymerization to produce a crosslinked polymer gel by free radical polymerization.

A reactive copolyester containing *exo*-methylene groups has been synthesized by carrying out ROP of 2-methylene-4-oxa-12-dodecanolide and DDL at 60 °C in toluene for 24 h.

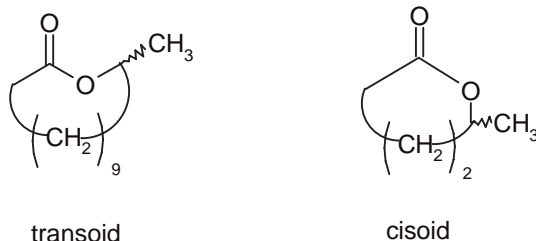


Figure 11.1 Transoid and cisoid conformations of the ester bond of ω -methylated lactones.

11.2.6

Enantioselective Polymerization

The enantioselective lipase CA-catalyzed copolymerization of racemic substituted lactones (β -butyrolactone) and achiral lactones (DDL) yielded *S*-enriched optically active copolymers with an enantiomeric excess (ee) of BL. The highest ee-value was achieved in the copolymerization of DDL with δ -caprolactone in isopropyl ether [77].

The Novozyme 435-catalyzed ring-opening of a range of ω -methylated lactones exhibited a switch from *S*- to *R*-selectivity on passing from small ring size to large-size lactones [78]. This effect was attributed to the transition of cisoid to transoid conformational preference of the ester bond on going from small rings (ring sizes ≤ 7) to large lactones (ring sizes ≥ 8) (Figure 11.1). The *S*-selectivity of the ring-opening of the small, cisoid lactones was low to moderate, while the *R*-selectivity of large transoid lactones was high. As a result, these lactones could be polymerized by kinetic resolution polymerization, yielding the enantiopure *R*-polyester with excellent enantiomeric excess (99%).

11.3

Physical Properties of Polymers

PCL is a semi-crystalline polymer with a degree of crystallinity of 50%, a low T_g (-60°C) and a melting point of 60°C . Injection-molded samples of PCL exhibited a modulus of 400 MPa and a yield stress of 15 MPa. Moreover, the material can be processed by injection molding, film blowing and extrusion. The rate of crystallization of PCL is slower than that of conventional polymers, while poly(ether-ester)s are more flexible due to the presence of ether linkages. Although PCL and poly(DXO) resemble each other in their chemical structure, PCL is semicrystalline whereas poly(DXO) is an amorphous polymer with a T_g of approximately -37°C [37].

Although, both crystallinity and melting temperatures can be significantly affected by copolymerization, the properties and potential applications of polymers derived from large lactones have not been investigated systematically. While the melting point of PCL (60°C) limits any applications that require its dimensional stability above room temperature, the larger lactones (with more than 10 methylene units per repeating unit) are expected to have higher melting points. Hence,

the properties of these polyesters are expected to lie somewhere between those of PCL and polyethylene.

The physical characterization of PDL was reported by Skoglund and Fransson [23, 24]. Although details of PDL synthesis were not reported, the molecular mass was low ($M_n \sim 5500 \text{ g mol}^{-1}$; PDI = 3.53), and the polymer melted in the temperature range of 82–89 °C (peak temperature 86 °C), with a T_g value ranging from –3 to –28 °C.

Previously, Lebedev *et al.* [79] had reported a melting temperature for PDL as 97.35 ± 1 °C, and an enthalpy of fusion 232.95 J g^{-1} , while some time later Zhong *et al.* [39] reported an enthalpy of 118.4 and 178.5 J g^{-1} at melting temperatures of 95 °C and 106 °C, respectively. No glass transition was detected within the temperature range studied from –100 to 130 °C, even after rapid quenching from the melt. These results revealed a large crystallization enthalpy in the differential scanning calorimetry (DSC) cooling traces, with only a minimal difference between the melting temperature and crystallization temperature being observed.

Recently, Focarete *et al.* [80] reported the physical properties and crystal structure [81] of PDL having a M_n of $64\,500 \text{ g mol}^{-1}$ and a PDI of 2. The polymer was prepared via a *Candida antarctica* lipase B (Novozyme 435)-catalyzed polymerization of PDL in toluene. The resultant polymer showed good thermal stability with a main thermogravimetric analysis (TGA) weight loss centered at 425 °C. The polymer was highly crystalline, and a T_g of –27 °C was detected only by using dynamic mechanical and dielectric spectroscopies. A melting temperature of 97 °C and heat of fusion of 140 J g^{-1} was reported. The degree of crystallinity, as calculated from DSC heat of fusion data, was 64%, and from wide angle X-ray diffraction measurements was 54%. The mechanical properties of the polymer were also investigated: the stress–strain curve showed the behavior of a hard and tough material. The elongation at break was from 100 to 200%, while the tensile strength was 14.5 MPa and the modulus 370 MPa.

The random copolyesters of PDL and CL were highly crystalline as a result of the cocrystallization of poly(PDL) and PCL [47]. The crystal phase was seen to melt at a temperature that changed linearly with the molar composition from that of the poly(PDL) homopolymer ($T_m = 97$ °C) and that of PCL (60 °C). Thus, copolyesters with a controlled density of hydrolyzable ester groups can be obtained having a wide range of melting points.

11.4

Summary and Prospects

In this chapter, we have described the various methods used to synthesize polyesters from large- and medium-sized lactones. Whilst enzymatic methods of polymerization seem preferable for the polymerization of large-ring lactones, both enzymatic and nonenzymatic methods may be used for medium-sized ring lactones. Although several polyesters and functional polyesters based on large lactones (rings containing 12 or more atoms) and medium-sized lactones (containing

7–11 atoms) have been synthesized, very few have achieved commercial success. Today, studies of the properties of polyesters derived from larger-ring lactones are still in their infancy, and further investigations are needed in order to increase the production of these materials so that their performance may be evaluated. Such polyesters represent a class of materials with controlled biodegradability, physical and mechanical properties that may, in time, be considered as a replacement for low-density polyethylene.

PCL, on the other hand, is a more versatile polymer that in the past has undergone extensive investigation for applications in agriculture and biomedicine, having also been widely used as mulch films, ropes or cups [2]. In order to control the properties and performance of PCL, a variety of copolymers with different lactones has been prepared. These have a controlled biodegradability and permeability, and can be obtained by judicious selection of the monomers. PCL has also been used in biodegradable drug-delivery systems, as the rate of its hydrolysis is much less than that of poly(DXO) or polylactide, thereby increasing its long-term suitability in this role.

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12

Polycarbonates

Helmut Keul

12.1

Introduction

Polymers having carbonate groups ($-\text{O}-\text{CO}-\text{O}-$) in the main chain—so-called polycarbonates—are carbonic acid esters of diphenols or diols and are therefore divided into poly(aromatic carbonate)s and poly(aliphatic carbonate)s. Technically, both classes of polymer are prepared via the polycondensation of carbonic acid derivatives with diphenols or diols, by a step-growth mechanism. The best-known polycarbonate-based plastic is one prepared from bisphenol-A and phosgene or diphenyl carbonate as the carbonic acid source. This polycarbonate is characterized as a very durable material with good optical and mechanical properties, and is appreciated for its high impact resistance, high transparency to visible light and excellent light transmission characteristics; hence, it is suitable for many technical applications. Poly(aliphatic carbonate)s are well-known biodegradable materials, and are employed for the development of specialty polymers. The ring-opening polymerization (ROP) of cyclic carbonates discloses an alternative route to polycarbonates, which follows a chain-growth mechanism comprising chain initiation and chain propagation with termination-, transfer- and transesterification reactions being absent in the ideal case (in this chapter, transesterification is considered as a synonym for transacylation; carbonates being considered as esters of carbonic acid). Under suitable conditions, the ROP of cyclic carbonates fulfils the prerequisites for a controlled polymer synthesis. Beside the molecular weight and molecular weight distribution, the polymer microstructure and the nature of end-groups, as well as polymer architecture, can be controlled [1–3].

The initial experiments on the ROP of aliphatic cyclic carbonates were performed shortly after Carothers and colleagues [4, 5] reported the preparation of these monomers with different ring sizes by depolymerization of the respective polycarbonates obtained via a polycondensation reaction. The ROP of aliphatic cyclic carbonates was first explored in the melt with potassium carbonate as initiator [6]. These polymers suffer from decarboxylation and, as a consequence, polycarbonates containing ether sequences are obtained. Aliphatic polycarbonates, however, were not considered to be useful materials for engineering thermoplastics, because of

their thermal instability and lack of ductility [7]. Aromatic cyclic carbonates based on bisphenol-A were synthesized by Schnell and Bottenbruch [8] in 1962 by the reaction of bisphenol-A-bischloroformate with bisphenol-A. At the same time, Prochaska [9] prepared cyclic carbonates with eight-membered rings, which were derived from *o,o'*-bisphenols obtained by the condensation of substituted phenols with formaldehyde. In recent years, the synthesis of aromatic cyclic carbonates has been optimized by research groups at General Electric and at Bayer AG, such that our understanding of the polymerization process has been improved. An overview of these results was presented by Brunelle under the title 'Preparation and Polymerization of Cyclic Carbonates' [7].

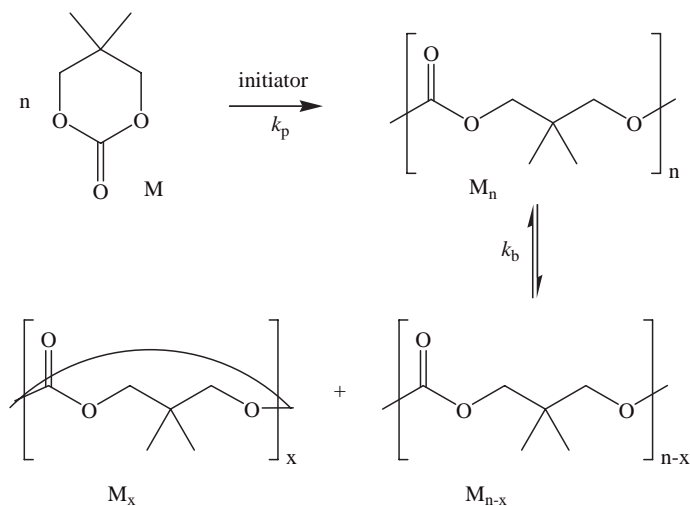
The recent most important finding in the field of polymerization of cyclic aliphatic carbonates has been the observation made by Takata and Endo, that cyclic carbonates polymerize with a considerable expansion in volume [10].

12.2

Polymerization of Cyclic Carbonates: Homopolymers and Block Copolymers

The ROP of cyclic carbonates with nucleophilic initiators is a chain reaction in which, besides initiation and propagation reactions, transesterification reactions must also be considered, with termination and transfer reactions being absent (Scheme 12.1) [3].

Intramolecular transesterification (back-biting) leads to cyclic oligomers, while intermolecular transesterification leads to a reshuffling of the repeating units with the consequence that, at equilibrium, a most probable distribution of the molecular weight is obtained. A good control of the reaction course is observed when the



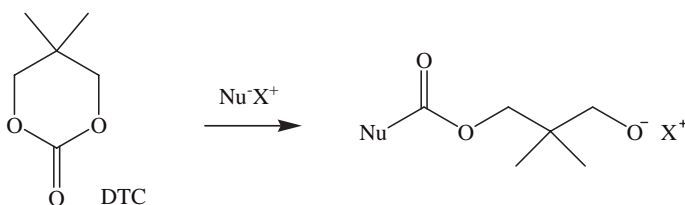
Scheme 12.1 Ring-opening polymerization of 2,2-dimethyltrimethylene carbonate (a model monomer for cyclic carbonates) with nucleophilic initiators: an equilibrium polymerization.

ratio of the rate constants of propagation (k_p) and of backbiting (k_b) and transesterification (k_{te}) are large, and termination and transfer reactions are absent. In other words, a high polymer yield and a narrow molecular weight distribution are obtained in the kinetically controlled regime of the reaction. To extend this, the polymerization conditions such as reaction medium (solvent and additives), temperature, monomer concentration and the nature of the active site must be adjusted. For example, with Li^+ and K^+ as counterions the polymerization rates are much higher than for Al or Zn in the active site [11–14].

12.2.1

Initiation

Cyclic carbonates such as 2,2-dimethyltrimethylene carbonate (DTC) are polymerized either anionically or by insertion in a ring-opening fashion with a variety of initiating systems based on alkali metals (Li, Na, K) [11], earth-alkali metals (Mg) [13], rare earth metals (La, Nd, Sm, Gd, Er, Y) [15–22], certain other metals (Al, Zn, Sn) [12, 14], and also with metal-free initiators [23] (Scheme 12.2).



Nu: carbanions, alcoholates

X: metals, tetrabutyl ammonium, tris(dimethylamino) sulfonium

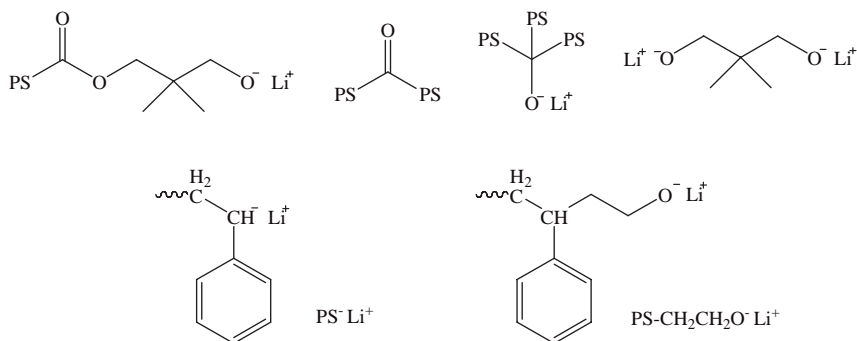
Scheme 12.2 Ring-opening polymerization of 2,2-dimethyltrimethylene carbonate (a model monomer for cyclic carbonates): initiation and formation of the active species.

The initiation reaction comprises the nucleophilic attack of the initiator at the carbonyl carbon, followed by an acyl–oxygen cleavage and formation of the active species, an alcoholate [24]. The efficiency of the initiation depends on the nucleophilicity of the initiator and on the electron affinity of the monomer: if both are high, then initiation is both fast and quantitative. A slow initiation leads to a broadening of the molecular weight distribution and a loss of molecular weight control.

12.2.1.1 Alkali Metal-Based and Metal-Free Initiators

Typical examples of initiators for cyclic carbonates—as shown for DTC—are alkali metal organic compounds such as *sec*-butyllithium (*sec*-BuLi), sodium- and potassium naphthalene, and lithium-, sodium- and potassium alkoxides or polymeric living vinyl or diene polymers with alkali metal counterions, as well as polymeric alcoholates. The use of these macroinitiators enables the identification of side reactions, as will be shown exemplarily for polystyrene lithium (PS^-Li^+) [25]. Besides the initiation reaction of PS^-Li^+ , which represents a site transformation of

a carbanionic to an alcoholate species, DTC also acts as a coupling agent for PS^-Li^+ to yield a polystyrene ketone and carbinol in addition to a dilithium diolate (Scheme 12.3). The latter may initiate the homopolymerization of DTC, whereas the 1:1 adduct of PS and DTC leads to an AB-block copolymer. Addition of the initiator to the monomer, which guarantees a high excess of monomer, minimizes side reactions; however, transformation of the polystyryl carbanion to result in a less-nucleophilic species avoids the side reaction. An appropriate reagent for lowering the nucleophilicity is ethylene oxide, while the addition of DTC to the alcoholate ($\text{PS}-\text{CH}_2-\text{CH}_2-\text{O}^-\text{Li}^+$) leads to high yields of AB-block-copolymers (Scheme 12.3).



Scheme 12.3 Initiation, side reactions and site transformation in ring-opening polymerization of 2,2-dimethyltrimethylene carbonate initiated by polystyrene lithium.

Both, sodium and potassium naphthalene, when used as electron-transfer reagents for the initiation of styrene polymerization, react with DTC as a nucleophile. The investigation of oligomers obtained in the initial stages of the polymerization by means of gel permeation chromatography (GPC) using a UV-detector revealed naphthalene to be incorporated into the growing chain.

Polymeric Li-, Na- and K-alcoholates were successfully used for the initiation of the polymerization of DTC. Thus, besides living vinylic or dienic polymers, hydroxy telechelic polymers of polyethylene oxide [26], poly(tetrahydrofuran) [27] and poly(dimethylsiloxane) [28] were transformed into their alcoholates by treatment with *sec*-BuLi or K-naphthalene, and used as initiators.

Anionic metal-free initiation was successfully applied to both aliphatic and aromatic cyclic carbonates [23, 29]. This method is based on the reaction of a silyl ether with fluoride anions, for example, tetrabutyl ammonium fluoride (Bu_4NF) or tris(dimethylamino)sulfonium trimethylsilyl difluoride (TASF, $[(\text{CH}_3)_2\text{N}]_3\text{SSi}(\text{CH}_3)_3\text{F}_2$), to produce an anion with a tetrabutyl ammonium or tris(dimethylamino)sulfonium counterion (Scheme 12.2). The metal-free system is an efficient initiator for DTC polymerization. The incorporation of the initiator in the polycarbonate was proven by GPC analysis of the polymer, which revealed a characteristic UV absorption when initiated with $\text{C}_6\text{H}_5\text{OCH}_2\text{CH}_2\text{O}^-\text{Bu}_4\text{N}^+$ [23].

12.2.1.2 Initiators for a Coordination–Insertion Mechanism

Similar results with respect to the initiation step were obtained with dibutyl magnesium [13], aluminum trialcoholates [14], dibutyltin dimethoxide [14], diethyl zinc [14], tin octoate and rare-earth metal compounds as initiators [15–22]. With these initiators, a coordination–insertion mechanism is active which, for some of the initiators, has been studied in detail [30, 31]. A special initiator with an aluminum alcoholate group is that of tetraphenylporphyrin aluminum; this has an alkoxy group as the third ligand (RO–Al–TPP) at the aluminum, and is known as the Inoue catalyst [32]. This initiator is active for various monomers, and is therefore used for the preparation of block copolymers with one or two polycarbonate blocks. Initiation occurs by the nucleophilic addition of RO–Al–TPP to the carbonyl group of the carbonate.

12.2.2

Chain Propagation

The polymerization of cyclic carbonates (M) is an equilibrium reaction, which proceeds in two steps (Scheme 12.4):



$$K = [P_{n+1}]/[P_n][M]_e \approx 1/[M]_e \quad (12.3)$$

$$\ln[M]_e = \Delta H^\circ/RT - \Delta S^\circ/R \quad (12.4) \quad K_x \sim x^{-5/2} \quad (12.8)$$

$$\Delta G^\circ = 0 \quad = > \quad T_c = \Delta H^\circ/\Delta S^\circ; \quad \Delta H^\circ < 0 \text{ and } \Delta S^\circ < 0 \quad (12.5)$$

Scheme 12.4 Equations with respect to the (i) monomer–polymer equilibrium (Equations 12.1–12.4); (ii) the ceiling temperature (Equation 12.5); and (iii) the ring–chain equilibrium (Equations 12.6–12.8).

- In the kinetically controlled regime, the chain propagation reaction is predominant and a high molecular-weight polymer (P_n) is formed (Equation 12.1). The monomer–polymer equilibrium (Equation 12.2) is characterized by the equilibrium constant (K) which is approximately equal to the inverse equilibrium monomer concentration ($[M]_e$) (Equation 12.3). Equation 12.4 relates the equilibrium monomer concentration and the free enthalpy of polymerization (ΔG°). For standard conditions ($[M]_0 = 1 \text{ mol L}^{-1}$) and above a critical temperature, no polymer is obtained. The critical temperature is defined as ceiling temperature (T_c) when both ΔH° and ΔS° are negative (Equation 12.5).
- In the thermodynamically controlled regime, back-biting reactions occur to form a low-molecular-weight fraction of cyclic oligomers (M_x) (Equation 12.6); a ring chain equilibrium is then established where K_x is the equilibrium constant,

which determines the concentration of the cyclic oligomer with degree of polymerization x (Equation 12.7). The equilibrium constant of an oligomer with degree of polymerization x (K_x) is approximately equal to the equilibrium concentration of that oligomer ($[M_x]_e$), and is proportional to the degree of polymerization to the -2.5 power (Equation 12.8).

Within the thermodynamically controlled regime, further intermolecular transesterification reactions occur, and from a starting Poisson distribution a Schulz–Flory distribution of the molecular weight is approached. The ratios k_p/k_b and k_p/k_{te} , where k_p is the rate constant of propagation, k_b the rate constant of back-biting and k_{te} the rate constant of the transesterification reaction, determine the selectivity of the reaction on the one hand and the microstructure of the polymer (in the case of copolymerization) on the other hand. The rate constants are determined by the monomer used and the nature of the active site.

12.2.2.1 Alkali Metal Alcoholate and Phenolate Active Sites

For alkali metal compounds used as initiators, the active species of polymerization was shown to be an alkali metal alcoholate for the aliphatic cyclic carbonates [24] and an alkali metal phenolate for the aromatic cyclic carbonates [29]. The time required to shift from kinetic control to thermodynamic control is about a few minutes when the polymerization of aliphatic cyclic carbonates is performed at 25 °C in toluene solution. The larger the alkali-metal counterion, the faster the polymerization and the smaller the selectivity parameter, $\beta = k_p/k_b$.

The aromatic cyclic carbonates based on bisphenol-A or substituted *o,o'*-methylenebisphenols were polymerized in tetrahydrofuran (THF) and in toluene with potassium-based initiators, for example potassium naphthalene at 60 °C and 25 °C, respectively [29]. In a rapid reaction the polymer was obtained in equilibrium with cyclic oligomers. However, with lithium-based initiators the chain propagation does not occur under these mild conditions, due to the low nucleophilicity of the active species, which arises from the covalent character of the lithium phenolate linkage.

Another point of interest with respect to the active species is the role of the chemical nature of the macroinitiator on the reaction course. For this, we have compared telechelic initiators based on poly(ethylene oxide) [PEO], poly(tetrahydrofuran) [PTHF] and poly(dimethylsiloxane) [PDMS]. The polymerization of DTC in toluene at 20 °C with the potassium salt of PEO with one terminal hydroxy group ($M_n = 1900 \text{ g mol}^{-1}$) as initiator [26] is a very rapid reaction in which, after only 30 s the reaction has passed the regime of kinetic control and is in the regime of thermodynamic control. The enhancement of the rate of propagation and of back-biting has its origin in an interaction between the potassium counterion and the PEO moiety. While the potassium ion is cryptated by the PEO coil, the hydroxylate end group of the growing poly(DTC) chain—for reasons of incompatibility—is ready to react with the carbonyl group of DTC or poly(DTC), with the result of chain growth, back-biting or transesterification. The complexation properties of PEO for potassium ions is well documented.

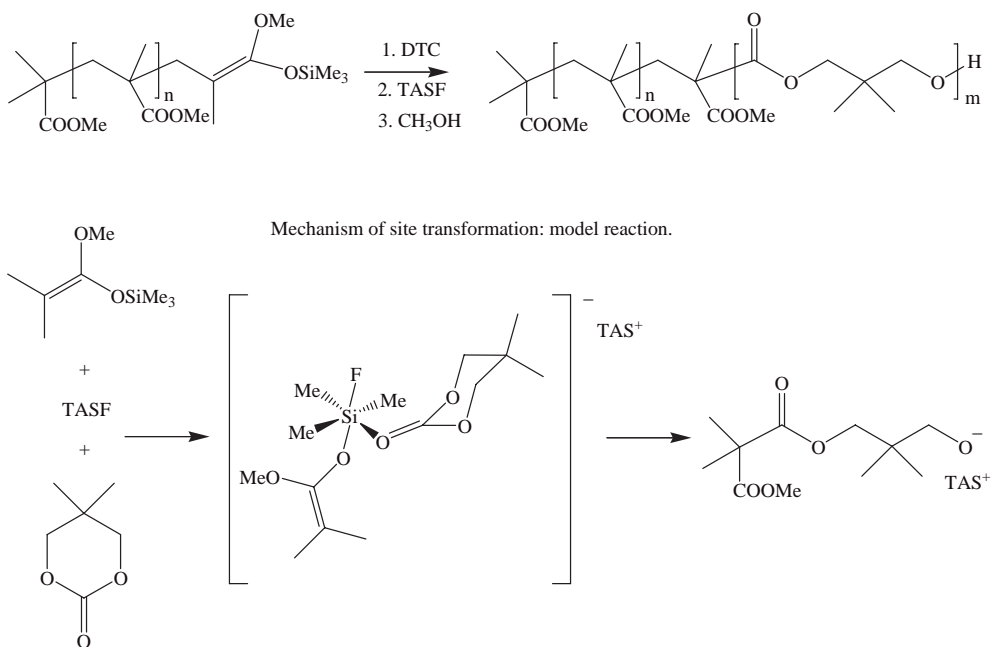
The nucleophilicity of the active species is significantly reduced by exchanging K^+ as counterion versus Li^+ . When using Li^+ as the counterion, high polymer yields were obtained after several minutes with a polydispersity index (PDI; M_w/M_n) = 1.3 and, in the case of PEO, a molecular weight of $10\,000\text{ g mol}^{-1}$. The lower nucleophilicity of the lithium alcoholate was ascribed to the more covalent character of the lithium–oxygen bond, as compared to the potassium–oxygen bond. Further Li^+ exerts only a low tendency for complexation with PEO, and self association prevails as compared to the corresponding potassium alcoholates.

The polymerization of DTC with polymeric initiators on the basis of poly(THF) was performed with different alcoholates as active species, and Li^+ , K^+ , or Bu_4N^+ counterions, in toluene solution at ambient temperature. The polymer yields were 80–90% with a PDI of $1.3 < M_w/M_n < 1.7$. Compared to the polymeric initiators based on PEO, the polymerization of DTC proceeded more slowly [27], a fact which could be explained by the reduced solvation ability of PTHF with respect to the counter ions, as compared to PEO.

The Li-salts of hydroxyl telechelic PDMS of molecular weight between 900 and $45\,900\text{ g mol}^{-1}$ were used as initiators for the DTC polymerization [28]. The polymerization time for the complete conversion of DTC was considerably larger than that with initiators based on PEO or PTHF and using Li^+ as counterion. Moreover, a dependence of the polymerization rate on the PDMS molecular weight was observed; for a given concentration of the active species the rate decreased with increasing molecular weight of the initiating block. The low polymerization rate of DTC with PDMS-based initiators has its origins in a decrease of the nucleophilicity of the active species being complexed by the PDMS chain. Such a complexation of an alcoholate has been reported, for example, in the reaction of diphenyl-diethoxy silane with potassium ethoxide. The dependence of the polymerization rate of DTC on the molecular weight of the initiator might be explained by the locally larger concentration of complexing $(CH_3)_3SiO$ moieties.

12.2.2.2 Metal-Free Active Sites: Site Transformation from Group Transfer Polymerization to Anionic Metal-Free Polymerization

When ‘living’ poly(methyl methacrylate) (PMMA) prepared by group transfer polymerization (GTP) is used as a macroinitiator for the ROP of cyclic carbonates, a site transformation from the silyl ketene acetal (GTP-mechanism) to an alcoholate (anionic ROP-mechanism) with a metal-free counterion occurs (Scheme 12.5). The GTP of PMMA was initiated with 1-methoxy-1-trimethylsilyloxy-2-methyl-1-propene (MTS) in combination with catalytic amounts of tetrabutyl ammonium cyanide in THF as solvent. Towards the end of the reaction, DTC is dissolved in the reaction mixture and 1 equiv. of fluoride anions (e.g. tris(dimethylamino) sulfonium difluorotrimethylsilicate; TASf), with respect to the active species, is added. In this way, good yields of the respective block copolymers were obtained. A model experiment for this site transformation is the polymerization of DTC with MTS as the initiator and TASf as the desilylating agent. The fluoride anion promotes desilylation of the silyl ketene acetal with formation of an enolate, which reacts as a carbon-centered nucleophile with the carbonyl carbon of DTC, thereby



Scheme 12.5 Site transformation of a trimethylsilyl ketene acetal active species to an alcoholate.

inducing ring-opening with formation of the alcoholate species and with tris(dimethylamino)sulfonium counterions [33].

12.2.2.3 Magnesium, Aluminum and Zinc Alcoholate Active Sites

With Bu_2Mg as initiator, the polymerization of DTC yields a product with a bimodal molecular weight distribution [13]—that is, a high-molecular-weight polymer and a low-molecular-weight fraction consisting of a homologous series of cyclic oligomers. This result is very similar to the ROP of DTC with alkali metal alcoholate active sites, where back-biting occurs. The polymerization of six-membered cyclic carbonates with Al- and Zn-based catalysts shows a high polymer yield at 25 °C (95%); even at 80 °C in toluene solution the extent of back-biting reactions is low [14]. This proves that, for Al and Zn in the active site, the propagation rate constant is considerably higher than the rate constant for back-biting reactions. Hence, within the scope of a kinetic treatment of the polymerization of DTC with $\text{Al}(\text{O-}i\text{-secBu})_3$ as initiator, only the propagation reaction must be considered [34]. A kinetic investigation of the polymerization of DTC with $i\text{-sec-BuLi}$ [35] and $\text{Al}(\text{O-}i\text{-secBu})_3$ [34] as initiators in toluene revealed a controlled polymerization—that is, monomer consumption according to first-order kinetics and a linear dependence of the number average molecular weight on conversion were observed. The rate constant for the polymerization of DTC with $\text{Al}(\text{O-}i\text{-secBu})_3$ at 24 °C was determined as $0.296 \text{ L mol}^{-1} \text{ s}^{-1}$. From the Arrhenius plot an activation energy of $E_a = 20.6 \text{ kJ mol}^{-1}$ was determined, which is smaller than that of the polymerization of ϵ -caprolactone ($E_a = 50.0 \text{ kJ mol}^{-1}$) [36].

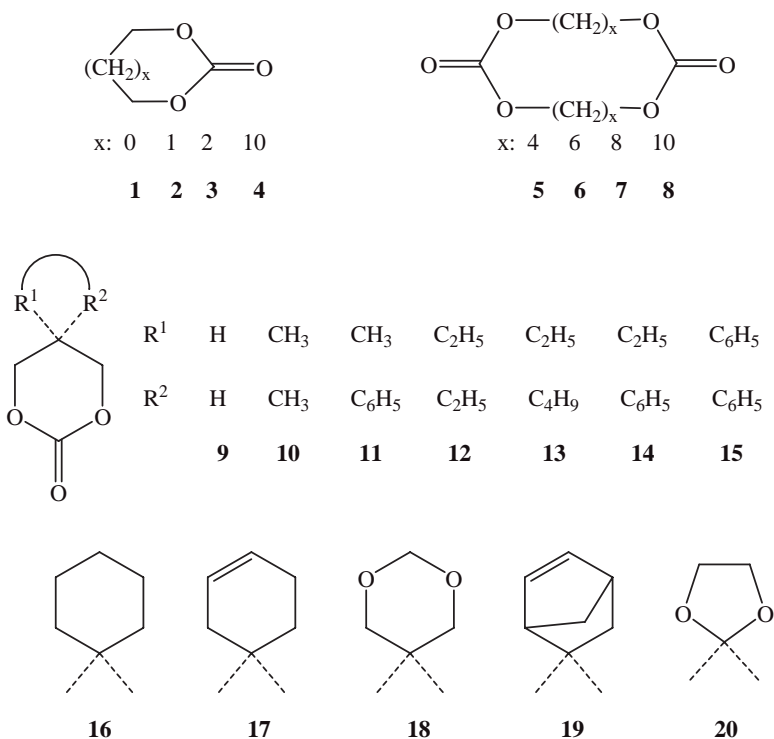
12.2.3

Monomers and Homopolymers

Monomers used for ROP are cyclic carbonates or cyclic dicarbonates of different ring sizes derived from α,ω -diols (Scheme 12.6).

While the ROP of five-membered cyclic carbonates is thermodynamically unfavorable and results in a poly(ether carbonate) via decarboxylation of part of the monomer [37], six-, seven- and higher-membered cyclic carbonates and dicarbonates [38–45] were polymerized to obtain polycarbonates without ether sequences. Several 2,2-disubstituted trimethylene carbonate and spirocarbonate monomers were prepared and polymerized in order to tune the polymer properties; highly crystalline materials or materials with variable T_g -values were obtained [46–56].

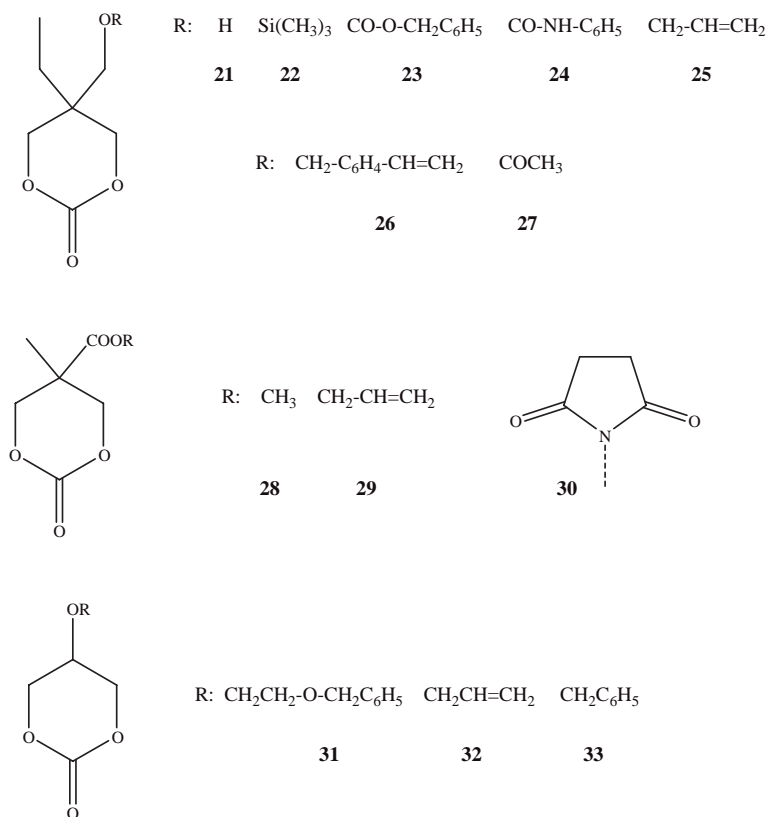
As mentioned above, since the ROP of cyclic carbonates is an equilibrium reaction, six-membered cyclic carbonates show a strong substitution effect on the equilibrium monomer concentration. The anionic ROP of 1,3-dioxan-2-one (**2**) and 5,5-disubstituted 1,3-dioxan-2-ones (**10**, **11**, **12**, **14**) in THF solution using potassium *tert*-butoxide as initiator revealed an increasing monomer concentration at



Scheme 12.6 Cyclic carbonates and dicarbonate monomers derived from α,ω -diols (**1**–**8**), 2,2-disubstituted 1,3-propanediols (**9**–**15**) and 2,2-spiro-1,3-propanediols (**16**–**20**).

equilibrium, with an increasing bulkiness of the substituents. This correlates well with the yields obtained in monomer synthesis (the reaction of 2,2-disubstituted 1,3-propanediols with phosgene dimer): the higher the steric demand of the substituents, the higher the selectivity towards the cyclic monomer in comparison to the linear oligomers. An estimation of the thermodynamic parameters reflected the polymerizability of the monomers ($\Delta H_p^0 = -26.37$ to -5.02 kJ mol⁻¹); a decrease in the absolute value of ΔH_p^0 is observed for monomers with increased bulkiness of the substituents. The reason for the decrease in polymerizability of the six-membered cyclic carbonates with increased bulkiness of the substituents lies in the conformational distortion of the polymer backbone, rather than in the change of conformation of the monomer caused by the substituents [49].

Several six-membered cyclic carbonates derived from 2-ethyl-2-(hydroxymethyl)propane-1,3-diol (**21–27**) [57–63], from 2,2-bis(hydroxymethyl)butanoic acid (**28–30**) [63–68], and from glycerol (**31–33**) [69–76] have been described (Scheme 12.7). In all cases, the *exo*-cyclic functional group (except the OH group in **21**) does not interfere with the active species, such that controlled polymerizations were



Scheme 12.7 Cyclic carbonate monomers derived from 2-ethyl-2-(hydroxymethyl)propane-1,3-diol (**21–27**), from 2,2-bis(hydroxymethyl)butanoic acid (**28–30**) and from glycerol (**31–33**).

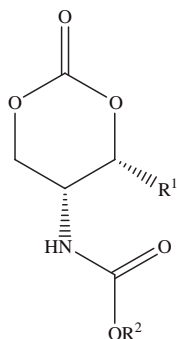
possible. Linear poly(2-ethyl-2-hydroxymethyltrimethylene carbonate) [poly(**21**)], which was not accessible via the anionic ROP of monomer **21** was obtained via polymer analogous reaction starting from linear poly(**22**) and poly(**23**), by hydrolysis or hydrogenation of the trimethylsilyl- and benzyloxycarbonyl protection groups [58]. Polycarbonates with allyloxymethyl and (*p*-vinylphenyl) methoxymethyl side groups—[poly(**25**)] and [poly(**26**)]—were successfully used for the preparation of crosslinked polymers [59, 62]. The crosslinked poly(**26**) was successfully de-crosslinked by treatment with potassium *tert*-butoxide in THF. For monomers with an *exo* cyclic ester group, such as **27**, **28**, **29** and **30**, reaction conditions were identified which allowed the preparation of linear polymers with a uniform microstructure; this means that an adventitious reaction of the active site with the ester-carbonyl group was avoided. Even a monomer having an activated ester substituent (**30**) was polymerized to obtain a linear polymer. Polymers containing this repeating unit were successfully converted with primary and secondary amines under mild conditions to obtain new functional polycarbonates [68].

A monomer with an allyl ester side-group (**29**) was successfully polymerized, and subsequently the C=C double bonds were epoxidized to produce new functional polycarbonates [67]. Polycarbonates based on glycerol were obtained via a thermal noncatalyzed ROP of 5-benzyloxy-1,3-dioxolan-2-one (**33**) and subsequent catalytic hydrogenolysis of the resulting poly(**33**). These polymers possess a hydrolyzable backbone, pendant hydroxyl groups suitable for polymer analogous reaction, and thus have tunable hydrophobic/hydrophilic properties [73, 76]. A novel type of glycerol-derived, water-soluble polycarbonate with pendant primary hydroxyl groups was obtained from 2-(2-benzyloxyethoxy)trimethylene carbonate (**31**) using the same sequence of the reactions described before [69].

L-Serine- and L-threonine-based cyclic carbonate monomers with benzyloxycarbonyl (Z) and *tert*-butyloxycarbonyl (Boc)-protected amine groups (**34**, **35**, **36**) (Scheme 12.8) were polymerized by ROP with lithium and potassium *tert*-butoxide as initiator. Although, the polymers obtained showed a specific rotation, the relatively low values suggested the absence of any higher-order structures. The Z and Boc protection groups were removed by hydrogenation and acid treatment, respectively, to afford the corresponding polycarbonates with free amino groups [77].

Polycarbonates with diethylene or triethylene glycol moieties were obtained by ROP of the corresponding cyclic dicarbonates **37** and **38**. These polymers are crystalline and hydrophilic, and suitable for the preparation of amphiphilic copolymers [78].

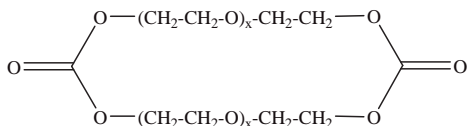
Despite the typical behavior of five-membered cyclic carbonates to result in polyether carbonates upon polymerization at higher temperatures ($T > 150^\circ\text{C}$), five-membered cyclic carbonates derived from methyl-4,6-*O*-benzylidene-glucopyranoside (**39**) [79] and 1,2-*O*-isopropylidene-D-xylofuranose (**40**) [80] were polymerized at temperatures below 70°C , without any elimination of carbon dioxide, to produce polycarbonates. The polymerization of **39** was carried out with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or potassium *tert*-butoxide, while that of **40** was performed with potassium *tert*-butoxide or yttrium isopropoxide as initiator. After removal of the protection groups, the carbohydrate polymers with carbonate main-chain linkages were obtained.



34: $R^1 = H$; $R^2 = CH_2C_6H_5$

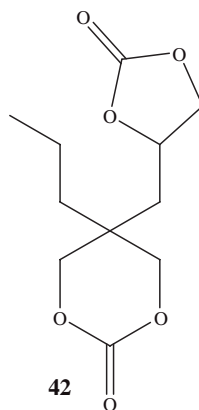
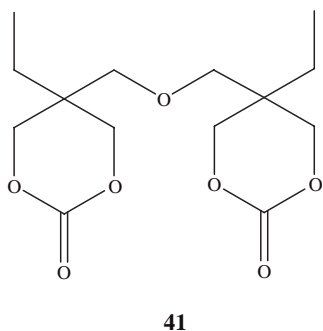
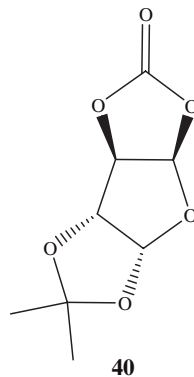
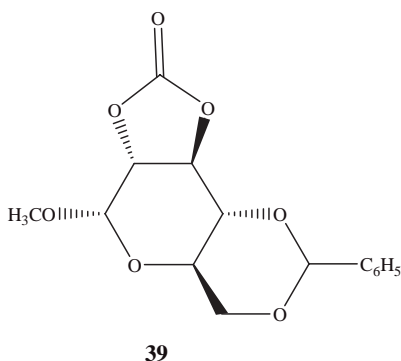
35: $R^1 = CH_3$; $R^2 = CH_2C_6H_5$

36: $R^1 = CH_3$; $R^2 = C(CH_3)_3$

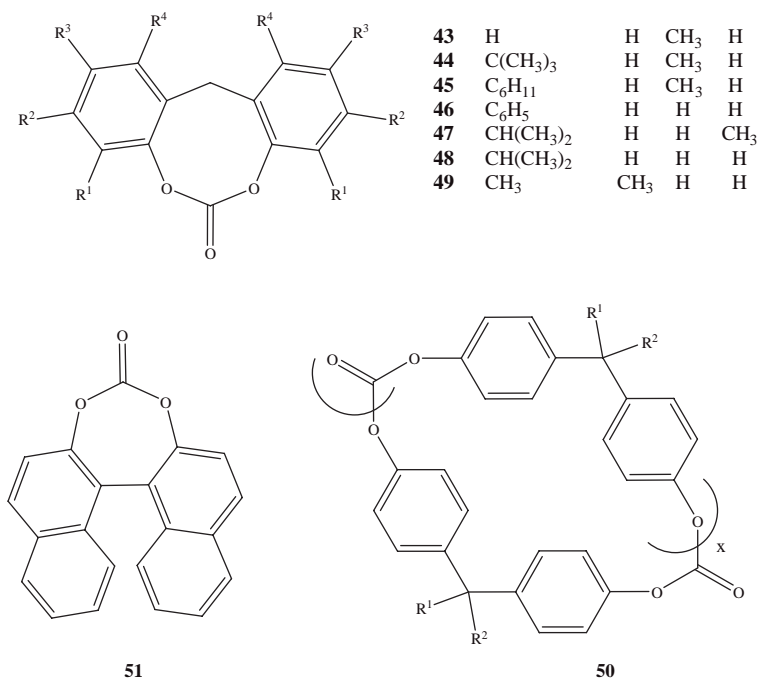


37: $x = 1$

38: $x = 2$



Scheme 12.8 Cyclic carbonate monomers derived from L-serine and L-threonine (**34–36**), from diethylene or triethylene glycol (**37, 38**), from glucopyranose (**39**) and D-xylofuranose (**40**) as well as bifunctional cyclic carbonates (**41, 42**).



Scheme 12.9 Cyclic carbonate monomers derived from *o,o'*-bisphenols (**43–49**), from *p,p'*-bisphenols (**50**) and from *o,o'*-bisnaphthol (**51**).

Bifunctional cyclic carbonates with two six-membered rings, as for example bis(5-ethyl-2-oxo-1,3-dioxan-5-yl)methylether (**41**), are used for the preparation of thermosetting aliphatic polycarbonates. These crosslinked polymers are degradable and have great potential for the preparation of delivery systems in agrochemical and medical applications [81].

Bifunctional cyclic carbonates consisting of both five- and six-membered rings were selectively polymerized by means of anionic ROP using DBU as initiator to afford a linear polycarbonate with five-membered cyclic carbonate groups in the side chain. This result provides experimental proof of the thermodynamic stability of the five-membered cyclic carbonate, and the thermodynamic instability of the six-membered cyclic carbonate. Further functionalization of these polymers by means of functional amines, which react with the cyclic carbonate groups but not with the linear open-chain carbonate groups, was performed to result in multifunctional polycarbonates [82].

Aromatic polycarbonates are produced technically from bisphenols via transesterification and interfacial phosgenation. In addition, ROP in the melt and solid-state polymerization has been developed, although not yet commercialized [83]. It has also been shown that the ROP of individual macrocycles based on bisphenol-A may progress without a catalyst [84] (Scheme 12.9).

The cyclic dimer was completely converted within 10 min at 300°C, whereas in the case of the trimer a small part remained unpolymerized even after 30 min at 300°C. The tetramer exhibits an even lower reactivity. Such lower reactivity is due to a slower initiation of the larger ring monomers. At this point, it should be noted that a mixture of cyclic monomers polymerizes much more rapidly than pure cyclic trimers or tetramers. Solid-state thermal polymerization produces a high-molecular-weight polymer ($M_w > 10^6$). Cyclic carbonates derived from *o,o'*-bisphenols 43–49 and of cyclic carbonates derived from *p,p'*-bisphenols, such as biphenol-A (50), were polymerized and copolymerized in solution using potassium naphthalene, potassium *tert*-butoxide or phenyl trimethylsilylether in combination with tris(dimethylamino)sulfonium trimethylsilyldifluoride as initiator [7]. From a practical viewpoint, these polycarbonates, which have high heat-deformation temperatures, may be used for moldings [85].

Due to the lower melt viscosity of the bisphenol-A cyclic carbonate monomers compared to that of the respective polycarbonates, and due to the low activation energy of polymerization, there exists a great potential for the preparation of inorganic organic hybrid materials starting with these cyclic aromatic carbonates. Both, polycarbonate carbon nanofiber composites and polycarbonate-layered silicate nanocomposites have been prepared using this procedure [86, 87].

12.2.4

Block Copolymers Comprising a Polycarbonate Block

Although block copolymers have been prepared using many of the above-mentioned monomers, for the preparation of block copolymers comprising a polycarbonate block it was necessary to follow different strategies:

- Sequential polymerization without site transformation: Block copolymers with two differently substituted polycarbonate blocks or a polycarbonate and a polyester block were prepared by sequential monomer addition, while the active site retained its character as an alcoholate. However, in order to obtain a high initiation efficiency and a narrow molecular weight distribution, the order in which the monomers are polymerized must be adjusted to correspond to the nucleophilicity of the active species and the electrophilicity of the monomer. The nature of the active site must also be chosen in such a way that transesterification, with the consequence of reshuffling of the monomers, is avoided; in other words, the ratios k_p/k_b and k_p/k_{te} must be very low.
- Sequential polymerization with site transformation: Block copolymers in which the active sites are not compatible are usually prepared in two steps. First, a site transformation is performed, after which initiation of the ROP occurs. Block copolymers with a poly(styrene) or a poly(butadiene) block and a poly(carbonate) block, for instance, are obtained after site transformation of a carbanionic to an alcoholate species [25]. The initiation reaction of the ROP of DTC using 'living' vinyl (or diene) polymers with alkali metal counterions as initiators, was performed after site transformation of the carbanionic into the alcoholate species

via reaction with ethylene oxide. When a living PMMA prepared by GTP was used as a macroinitiator, site transformation from the silyl keteneacetal (GTP) to an alcoholate (anionic ROP) with a metal-free counterion was performed before ROP of the cyclic carbonate occurred [33]. The use of macroinitiators in the polymerization of cyclic carbonates results in A–B or B–A–B block copolymers, depending on the functionality of the macroinitiator used to prepare the A-block. An analysis of the resultant polymeric product provides information on the efficiency of the site transformation reaction, and also on side reactions.

- Polymerization of cyclic carbonates using activated hydroxyl telechelic polymers: Another strategy for the preparation of block copolymers with a polycarbonate block is the use of suitable polymers with one or two hydroxyl end-groups as initiator for the ROP. The hydroxyl groups are transformed into alcoholate groups to initiate the anionic ROP. The monofunctional macroinitiators result in A–B block copolymers, and the bifunctional macroinitiators in B–A–B block copolymers, where A represents the macroinitiator block and B the polycarbonate block(s). Bifunctional macroinitiators based on PEO, PTHF and PDMS were applied for the ROP of DTC, and good yields of B–A–B block copolymers were obtained. The rate of polymerization is clearly influenced by the chemical nature of the macroinitiator: an enhancement in the rate was observed for the PEO-macroinitiator, retardation was observed for the PDMS macroinitiator, while for the PTHF macroinitiator no influence on the rate was observed [26–28]. The explanation for such rate enhancement is solvation of the cation by the PEO chain, which leads to an increased nucleophilicity of the alcoholate. The retardation of polymerization rate has its origin in the complexation of the alcoholate by the PDMS chain, with the result of a pentacoordinated silicon atom that is associated with a decrease in nucleophilicity.

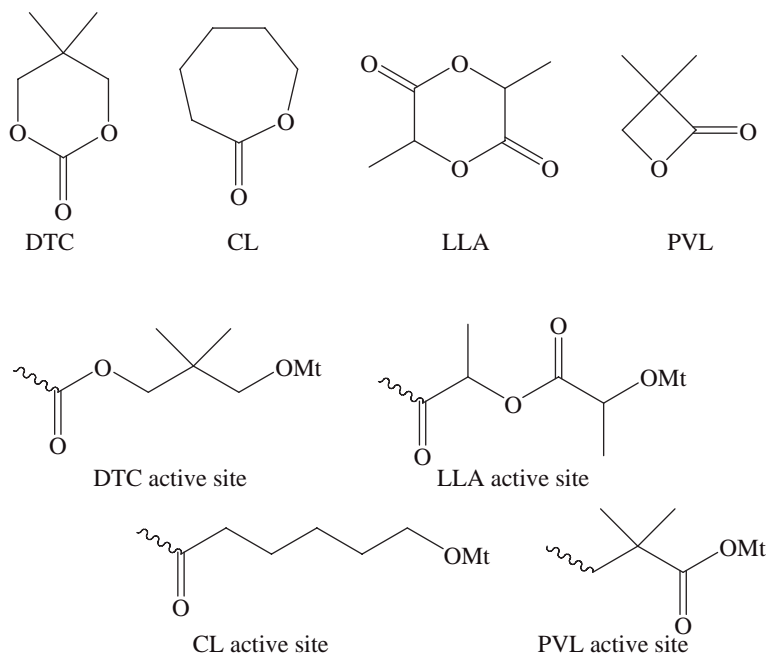
12.2.5

Copolymerization of Cyclic Carbonates with Lactones

The copolymerization of mixtures of cyclic carbonates and lactones has been described for several monomers, and may result in random, tapered and—in special cases—block copolymers. DTC was copolymerized with ϵ -caprolactone (CL), pivalolactone (PVL) and L,L-lactide (LLA). The active species for the homopolymerization were determined to be the alcoholates for DTC, CL and LLA, and the carboxylate for PVL (Scheme 12.10).

The sequential copolymerization of DTC and CL with a variety of initiating systems results in block copolymers, if the conditions are carefully chosen so that transesterification is suppressed, for example, with Mg- and Al-based initiators [12–14]. For these copolymers, only DTC–DTC and CL–CL homodiads were detected in the ^{13}C NMR spectrum.

The copolymerization of a mixture of DTC and CL at low temperatures resulted in A–X–B-type copolymers, where A was a PDTC block, B a PCL block, and X a tapered sequence of DTC and CL repeating units. As a consequence, DTC–CL and CL–DTC heterodiads were observed in the ^{13}C NMR spectra. The concentration of

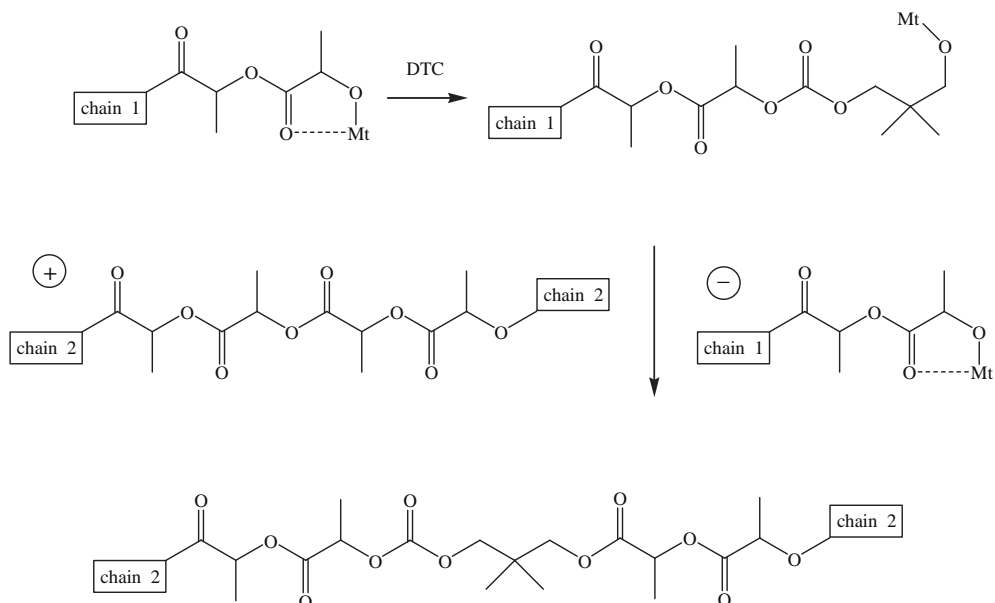


Scheme 12.10 Cyclic carbonate and lactone monomers and their active sites in nucleophilic ring-opening polymerization.

heterodiads was seen to increase with temperature such that, at 80 °C, a random copolymer was obtained. From a mechanistic point of view, the active species of each monomer would be eligible to react with both DTC and CL. Due to the fact that, with Mg, Al and Zn in the active site, transesterification plays a minor role, the microstructure of the copolymers prepared with these active sites is determined by the nucleophilicity of the active species and the electrophilicity of the monomer alone. For Li, K and Sn in the active site, a reshuffling of the monomers via transesterification determines the final polymer microstructure, beside the copolymerization parameters, especially at higher temperatures [88].

The copolymerization of a mixture of DTC and PVL in toluene as a solvent and with K-naphthalin as the initiator resulted in an A–B block copolymer, where A was the PDTC block and B the PPVL block [88, 89]. This became evident by ^{13}C NMR analysis, where only signals corresponding to homodiads were observed. The explanation for this ‘one-pot’ block copolymer synthesis is based on the large difference in the rate of polymerization of DTC and PVL, combined with the incompatibility of the active species (K-carboxylate does not react with DTC monomer), and with the fact that no transesterification occurs between the ester and carbonate groups. It should be noted that with initiators based on Li, Mg, Al, Zn and Sn, no copolymers were obtained.

The sequential copolymerization of DTC and LLA [88, 90] revealed different polymer microstructures, depending on the order in which the monomers were added to the initiator. The polymerization of first LLA followed by the addition of



Scheme 12.11 Mechanism of copolymerization of DTC with LLA.

DTC to the 'living' PLLA* resulted in a random copolymer, whereas the addition of LLA to a 'living' PDTC* resulted in a block copolymer. The microstructure of these copolymers was evident from the ^{13}C NMR spectra. The copolymerization of a mixture of LLA and DTC also resulted in a random copolymer (Scheme 12.11).

According to time-dependent ^1H NMR analysis, initially only LLA–LLA diads are formed—that is, at first the LLA is polymerized. However, as time elapsed, triads comprising one DTC and two LLA units were formed, then triads with two DTC and one LLA unit, and finally DTC–lactate–DTC triads and DTC–DTC diads were formed. For a mechanistic proposal, two further experimental observations should be taken into consideration: (i) A mixture of 'living' PLLA* and 'living' PDTC* showed no transesterification, such that after 12 h at 90°C no mixed diads were observed; and (ii) living PDTC–block–PLLA* and PLLA–stat–DTC* showed no changes in microstructure under conditions suited to polymerization.

Based on these results, the following mechanism was proposed (Scheme 12.11). First, LLA is polymerized, after which the active PLLA* species is well stabilized by the $-\text{M}$ effect of the adjacent carbonyl group (enol formation) and by the formation of a five-membered cyclic complex including the metallic species. Upon reaction of the PLLA* active species with DTC, the newly formed active site has a reduced capability of stabilization. The most electrophilic species in the system capable of reacting with the active species is the ester group of a LLA–LLA diad in the polymer chain. Hence, by this reaction, the active LLA site is regenerated and an LLA–DTC–LLA triad formed. In conclusion, the insertion of DTC into an LLA–LLA diad is formally realized, and the process is then repeated until all DTC is incorporated into the polymer.

12.3

Summary and Prospects

Cyclic carbonate monomers with a variety of functional groups have been prepared and polymerized by means of ROP. Compared to other cyclic monomers, such as cyclic ethers and esters, the diversity of functional monomers is much greater within the cyclic carbonates, and not only the polymer microstructure and architecture but also the molecular weight and molecular weight distribution may be well controlled. Copolymers comprising blocks of different chemical structure were prepared, and the site transformation was carefully studied for several types of active species.

Recent developments in organocatalytic pathways for the ROP of lactide and several lactones, without adverse transesterification creating polymers that are metal-free and therefore perfect candidates for biomedical and microelectronic applications, have been developed using *N*-heterocyclic carbenes, thiourea-tertiary amines, and amidine and guanidine bases. Here, the exquisite control, the absence of metal ions, the ready synthetic availability of the catalysts, and the mild reaction conditions are of major importance for tailor-made polyesters, and also have high potential for functional polycarbonates [91, 92].

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13

Polymerization of Cycloalkanes

Jacques Penelle

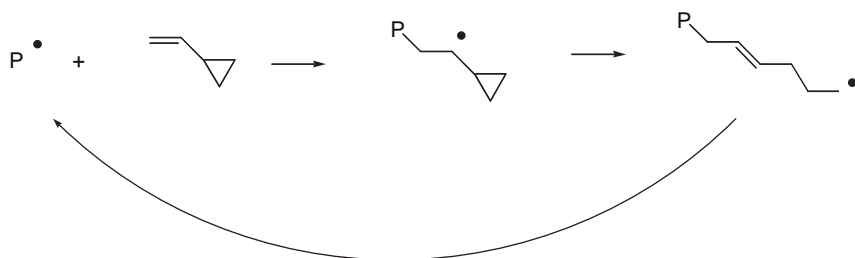
13.1

Introduction

The type of ring-opening polymerization (ROP) described in this chapter focuses on monomers whose cycle is opened via the direct rupture of a carbon–carbon single bond during the propagation step. As such, it does not include metathesis polymerizations, which involve C=C double bonds (these are treated separately in Chapter 8). Neither does it deal with monomers for which the cycle is appended to a polymerizable moiety, such as in vinyl cyclopropanes (for examples, see Refs [1, 2]). Indeed, in this latter case the cycle breaks indirectly due to a rapid rearrangement of the α -cycloalkyl-substituted propagating center (see Scheme 13.1), and not from the direct attack of the propagating center on one of the C–C bonds of the cycle.

Thus circumscribed, the total number of publications covering the present topic amounts to less than 200 references, a number that pales when compared to the literature on hand for a *single* heterocyclic monomer such as ethylene oxide. Yet, the body of experimental evidences accumulated when examining specific monomers is large, with about a hundred monomers investigated thus far. As a result of the large spectrum of structures examined during the past half-century, a few structure–reactivity relationships can be drawn, opening the way to the design of more efficient polymerization conditions or more reactive monomers of this type. In addition, a few monomers have shown superior polymerizabilities, including the possibility to control architectures via ‘living’ polymerization techniques [3, 4], or have led to polymers with remarkable properties, maintaining a steady amount of interest expressed in this research area and a stable number of new contributions over time.

An attempt will be made in this chapter to review those structural parameters that play a critical role in the ROP of cycloalkanes. First, the thermodynamic parameters that govern the polymerizability of these monomers as a class will be briefly analyzed after which details of the various cycloalkyl monomers whose polymerizations have been described in the literature will be provided. For this, we will use mostly tabulated data.



Scheme 13.1

It should be noted that reviews covering specific areas of this chapter have appeared periodically [5, 6], dealing mostly with their authors' findings on the polymerization of bicyclobutanes [7–9], cyclopropanes [1, 3, 10–12] and propellanes [13–16]. These reviews are highly recommended as a further source of information, not only for the polymerization of monomers but also for the properties of the polymers thus obtained.

13.2

General Overview and Thermodynamic Requirements

Molecules with structures that possibly match the monomer as defined above—that is, a cyclic system with at least one C–C bond—are most likely among the most frequent structures of organic chemistry. A casual browse through most chemical catalogues would lead to hundreds of possible matches, with widespread natural products such as steroids contributing to make this number even higher. Based on this extensive availability, it is not surprising that cycloalkanes were among the first molecules to be tested as putative monomers in the history of polymer chemistry. One of the first ever claims for a successful polymerization (in 1936) [17]—but which unfortunately proved later to be incorrect [18]—involved cyclopropane (CH₂)₃, the smallest member of the monocyclic series. In addition, one of the very few reports of the nineteenth century's literature with reasonable experimental evidences that a ROP had occurred also involved a cyclopropane, namely diethyl cyclopropane-1,1-dicarboxylate [19].

Nonetheless, and in sharp contrast to the polymerization of heterocycles, such achievements—as measured by the number of new structures added to the pool of available monomers—have been somewhat limited. This success rate is not surprising in itself if one considers the difficulty of the reaction involved, namely a C–C bond cleavage. Carbon–carbon single bonds are notoriously difficult to break: as a rule, they do not react with free-radicals and rarely participate in reactions with electrophiles and nucleophiles [20]. In addition, as the two atoms making the bond are identical, no polarization is introduced into the system,

making ionic reactions with nucleophiles or electrophiles more difficult. As a result, reactivity can only be expected:

- when the ‘normal’ overlap of atomic orbitals in the C—C σ link is severely disturbed by geometric parameters, introducing an unusual amount of biradical character in the single bond (e.g. in bicyclobutanes, propellanes and other highly strained polycyclic systems) [21]
- when substituents are introduced on at least one of the two carbons, thereby increasing the bond polarity and introducing some zwitterionic nature into the bond [20].

In addition, thermodynamics plays an important role. The basic thermochemical parameters are summarized in Figure 13.1 for the polymerization of simple cycloalkanes (CH_2)_x leading to poly(methylene). The data present the ‘theoretical’ free energy of polymerization (ΔG°) at 25 °C as a function of the cycle size (the first data point corresponds to the polymerization of ethylene) [22]. The results were calculated based on the thermochemical parameters of the putative monomers and of poly(m)ethylene. With the exception of cyclohexane, all cycloalkanes display negative free energies of polymerization. Noteworthy in this regard is the very low ΔG° obtained for cyclopropane and cyclobutane, with free energies of polymerization even lower than for ethylene.

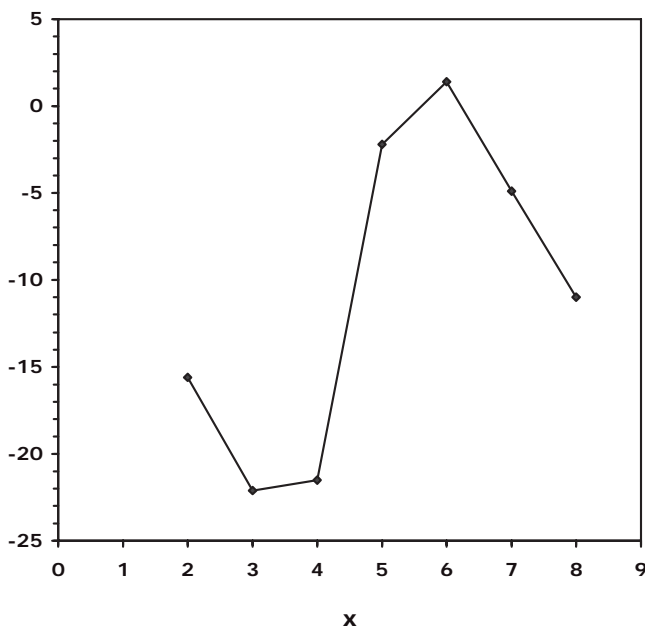


Figure 13.1 Free-energy of polymerization at 25 °C for the ring-opening polymerization of unsubstituted cycloalkanes (CH_2)_x [22].

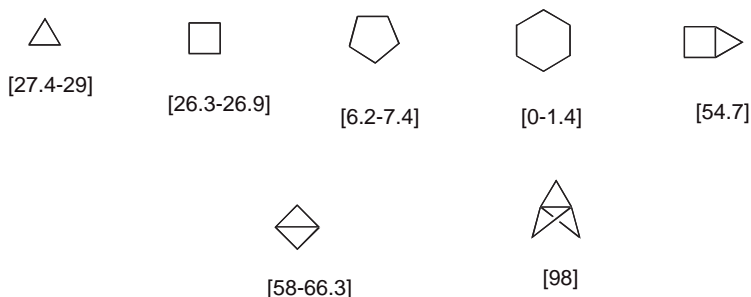


Figure 13.2 Examples of cycloalkanes with corresponding strain energies expressed in kcal mol⁻¹ [23].



Further strain can be introduced into polycyclic systems by incorporating several rings (especially three- and four-membered cycles) into the molecular structure. A few examples of such atomic arrangements are included in Figure 13.2, along with the corresponding strain energy. It must be realized, however, that the ring-opening of one bond in these systems—typically the most strained one—does not release the entire strain energy. When the ring opening has occurred, cyclic architectures are often maintained, as exemplified by the ring opening of [1.1.0]bicyclobutanes whose central C—C bond breaks, but maintains a cyclobutyl structure (Scheme 13.2).

13.3

Structure–Reactivity Relationships Based on a Comprehensive Survey of the Current Literature

An attempt is made in this chapter to document, as exhaustively as possible, the monomers that fit the above definition of a cycloalkane ROP. In order to summarize the key information, a thorough examination of the literature was made, and a tabular arrangement used to summarize the results (see Tables 13.1 to 13.7), with the monomers placed in categories (cyclopropanes, cyclobutanes, bicyclobutanes, propellanes), then into several subcategories when needed (coordination/cationic, anionic, free-radical, etc.). When known, the C—C bond being broken was indicated for polycyclic systems.

The limitation of such an exercise is that the data mixes records of quite different nature: from short notes claiming a molecule polymerized with no or little evidences for the fact, to exhaustive studies including methodical structural analysis, careful molecular weight determinations, and full mechanistic investigations. However, by keeping this warning in mind, a few general comments can be made, albeit with caution.

Table 13.1 Anionic polymerization of electrophilic cyclopropanes.

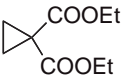
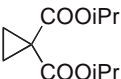
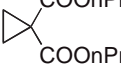
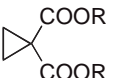
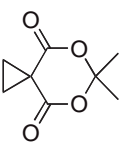
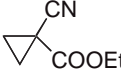
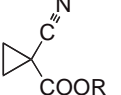
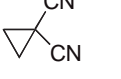
Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
1		(a) $\text{CH}_3\text{CH}(\text{COOEt})_2$ or $\text{CH}_2(\text{COOEt})_2$, sodium ethanolate, 80–100°C, 8 h; (b) $\text{Na}/\text{CH}_2(\text{COOEt})_2$; (c) PhSNa , 80–130°C	Polymerization observed; living polymerization possible	(a) [19, 24]; (b) [25]; (c) [26]
2		PhSNa , DMSO, 130–200°C	Living polymerization observed	[27–30]
3		PhSNa , DMSO, 130°C	Living polymerization observed	[31]
4	 R = Me, Et, nPr, nHex, Bz	PhSNa , DMSO, 80–200°C	Polymerization observed	[29]
5		PhSNa , DMSO, RT	Oligomers	[29]
6		PhSNa , DMSO (few experimental details)	Polymerization observed	[29]
7	 R = Et, iPr, nBu, n-octyl	(a) PhSNa , DMSO, 60°C; (b) PhSM (M = Li, Na, K, NBu_4), DMSO, 60°C; (c) DMSO, 60°C, various amines (NMP, DBU, Et_3N , pyridine); (d) PhSNa , DMSO, 60–120°C	Polymerization observed, with some living character	(a) [32]; (b–d) [33]
8		(a) PhSNa , DMSO, RT to 60°C; (b) DMSO, 30–60°C, various initiators: PhSM (M = Na, K), NaCN , $\text{CH}_3\text{C}(\text{COOEt})_2\text{Na}$, amines)	Polymerization observed	[29, 34]

Table 13.1 Continued

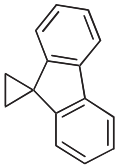
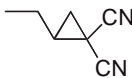
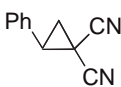
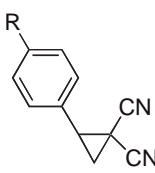
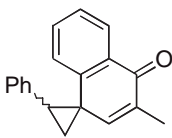
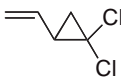
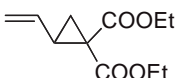
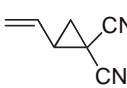
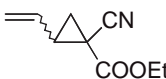
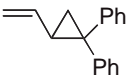
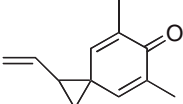
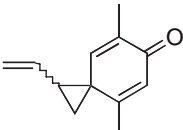
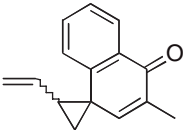

Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
9		Fluorenyl lithium, DMPU or HMPA, $T > 100^\circ\text{C}$	ROP observed	[35]
10		NaCN, DMF, 25°C	No polymerization	[36]
11		NaCN, DMF, 8°C	Polymerization observed	[36]
12	 R = H, Me, OMe, NO ₂ , Cl	NaCN or pyridine, DMF, $10\text{--}35^\circ\text{C}$	Polymerization observed	[37]
13		NaCN, DMF, -20 to 40°C	ROP observed	[38]
14		<i>n</i> BuLi, 40°C , 20 h	Polymerization observed (limited evidence)	[39]
15		NaCN, DMF, RT	No polymerization observed	[40]
16		NaCN, DMF, $0\text{--}15^\circ\text{C}$	ROP observed, no polymerization of the C=C bond	[36, 40]
17		NaCN, DMF, $7\text{--}25^\circ\text{C}$	ROP observed, no polymerization of the C=C bond	[40]

Table 13.1 Continued

Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
18		NaCN, DMF, RT	No polymerization observed	[40]
19		NaCN, DMF, –20 to 28 °C	ROP observed, no polymerization of the C=C bond	[38, 41]
20		NaCN, DMF, –20 to 70 °C	ROP observed, no polymerization of the C=C bond	[38, 41]
21		NaCN, DMF, –20 to 80 °C	Ring-opening polymerization observed, no polymerization of the C=C bond	[38, 41]
22		NaCN, DMF, 0 °C	No polymerization	[36]

DMSO = dimethyl sulfoxide; DMF = dimethyl formamide; DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene; DMPU = 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone; HMPA = hexamethylphosphoramide; RT = room temperature.

Table 13.2 Cationic polymerization of nucleophilic cyclopropanes.




Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
1		(a) AlBr ₃ /HBr, heptane, –78 °C to 0 °C, (b) BF ₃ (gas), CH ₂ Cl ₂ , 80 °C, (c) Et ₃ Al/TiCl ₄ , 20–80 °C	Oligomers	(a) [42]; (b–c) [43]
2		AlCl ₃ /HCl, 25 °C	Polymerization claimed	[44]
3		AlBr ₃ /HBr or AlCl ₃ , 24 °C	Polymerization claimed	[44]

Table 13.2 Continued










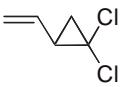
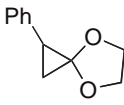
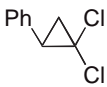
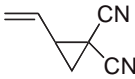
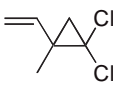
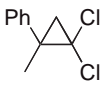

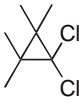

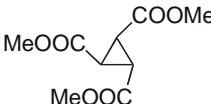
Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
4		AlBr_3 , -50 to -10°C	Oligomers	[45]
5		(a) Ziegler catalyst, (b) AlBr_3 , 0°C , <i>n</i> -hexane; (c) $\text{EtAlCl}_2/\text{TiCl}_3$, <i>n</i> -heptane, RT, 18 days	Oligomers	(a) [46]; (b–c) [47]
6		AlCl_3 , CH_2Cl_2 , -80°C	Polymerization observed	[48]
7		$\text{Al}(\text{OH})\text{Cl}_2$, 24°C	Polymerization claimed	[44]
8		(a) AlBr_3 or AlBr_3/HBr , -50 to 24°C ; (b) AlBr_3 , -50 to 0°C ; (c) AlBr_3 , 0°C , various solvents; (d) $\text{EtAlCl}_2/\text{TiCl}_3$, <i>n</i> -heptane, RT, 18 days	Oligomers	(a) [44]; (b) [49]; (c–d) [47]
9		(a) AlX_3 ($\text{X} = \text{Cl}, \text{Br}$), CH_2Cl_2 , -80°C ; (b) various cationic initiators: $\text{BF}_3 \cdot \text{OEt}_2$, AlCl_3 , TiCl_4 , SnCl_4 , ZrCl_4 , MoCl_5 , WCl_6 ; (c) CH_2Cl_2 or hexane, 80°C , various coordination catalysts: $\text{Et}_3\text{Al}/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $\text{Et}_3\text{Al}/\text{WCl}_6$, $\text{Et}_2\text{AlCl}/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $(i\text{Bu})_3\text{Al}/\text{SnCl}_4$	Polymerization observed, complex structure	(a) [48]; (b–c) [50–52]
10		AlBr_3 , EtCl , 35 – 40°C	Polymerization observed	[49]
11		AlBr_3 , EtCl , 35 – 40°C	Polymerization observed	[49]
12		Various initiators: $\text{BF}_3 \cdot \text{OEt}_2$, I_2 , TiCl_4 ..., $\text{AlEt}_3/\text{TiCl}_4$, $\text{AlEt}_3/\text{VCl}_3$...	Polymerization of the conjugated diene observed; <u>no opening of the cyclopropyl ring</u>	[53]
13		(a) Various cationic/coordination initiators (no experimental details): $\text{BF}_3 \cdot \text{OEt}_2$, AlCl_3 , TiCl_4 , $\text{Et}_3\text{Al}/\text{TiCl}_4$; (b) $\text{TiCl}_3/\text{Et}_3\text{Al}$, <i>n</i> -heptane, 50°C	(a) No polymerization; (b) oligomers of complex structure with ring-opening observed	(a) [54]; (b) [55]

Table 13.2 Continued

Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
14		Cationic initiators: (a) $\text{BF}_3 \cdot \text{OEt}_2$, CHCl_3 , -10°C , (b) $\text{CF}_3\text{SO}_3\text{CH}_3$, -76 or 25°C , CH_2Cl_2	Oligomers; rearrangement of the propagating carbocation	[56]
15		$50\text{--}80^\circ\text{C}$, <i>n</i> -hexane, various initiators $\text{Et}_3\text{Al}/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $\text{Et}_2\text{AlCl}/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $\text{EtAlCl}_2/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $i\text{Bu}_3\text{Al}/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $\text{Et}_3\text{Al}/\text{RhCl}_3$, few experimental details	Oligomers of complex structure; dehalogenation occurs simultaneously	[57]
16		Cationic (experimental conditions not detailed)	Failed	[58]
17		(a) $50\text{--}80^\circ\text{C}$, <i>n</i> -hexane, various initiators: $\text{Et}_3\text{Al}/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $\text{Et}_2\text{AlCl}/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $\text{EtAlCl}_2/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $i\text{Bu}_3\text{Al}/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $\text{Et}_3\text{Al}/\text{RhCl}_3$, few experimental details; (b) Various initiators: TiCl_4 , SnCl_4 , WCl_6 , 80°C	Oligomers of complex structure with ring-opening observed; dehalogenation occurs simultaneously	(a) [57]; (a–b) [50, 59, 60]
18		$50\text{--}80^\circ\text{C}$, <i>n</i> -hexane, various initiators $\text{Et}_3\text{Al}/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $\text{Et}_2\text{AlCl}/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $\text{EtAlCl}_2/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $i\text{Bu}_3\text{Al}/\text{MCl}_4$ ($\text{M} = \text{Ti}, \text{Sn}$), $\text{Et}_3\text{Al}/\text{RhCl}_3$, few experimental details	Oligomers of complex structure; dehalogenation occurs simultaneously	[57]
19		(a) AlCl_3 , -78°C to 0°C ; (b) AlCl_3 , RT; (c) $\text{Et}_3\text{Al}/\text{TiCl}_4$ or $\text{Et}_2\text{AlCl}/\text{TiCl}_4$, $50\text{--}80^\circ\text{C}$, <i>n</i> -hexane	Oligomers of complex structure; dehalogenation occurs simultaneously	(a) [61]; (b) [62]; (c) [57]
20		$\text{Et}_3\text{Al}/\text{TiCl}_4$ or $\text{Et}_2\text{AlCl}/\text{TiCl}_4$, $50\text{--}80^\circ\text{C}$, <i>n</i> -hexane	No polymerization	[57]

RT = room temperature.

Table 13.3 Polymerization of cyclopropanes according to poorly defined or disputable mechanisms.

Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
1		Mercury-photosensitized UV irradiation of gaseous cyclopropane	Oligomerization observed; proved [18] not to result from a ROP as originally thought [17, 63, 64]	[17, 18, 63, 64]
2		(a) HBr, 30 °C, various solvents; (b) HBr/AlBr ₃ , 30 °C, CH ₂ Cl ₂ ; (c) AlBr ₃ , 65 °C, bulk; (d) CF ₃ COOH, 30 °C, CH ₂ Cl ₂ ; (e) SnCl ₄ , 30 °C, CH ₂ Cl ₂ ; (f) <i>p</i> TosOH, 30 °C, CH ₂ Cl ₂ ; (g) SnCl ₄ , SO ₂ or bulk, –50 or 65 °C; (h) HgCl ₂ , 65 °C, <i>n</i> PrCN; (i) MeONa, 5-crown-5, –50 °C, CHCl ₃ ; (j) <i>n</i> BuLi, –40 °C, CHCl ₃ ; (k) LiAlH ₄ , 65 °C, <i>n</i> PrCN; (l) piperazine, 65 °C, <i>n</i> PrCN; (m) AlEt ₃ /TiCl ₄ , toluene, 30 °C; (n) AIBN, 65 °C, bulk; (o) AIBN, Br ₂ , 65 °C	Polymerization observed exclusively under conditions (a–b); i.e. in the presence of HBr, consistent with a ring-opening mechanism; no polymerization under conditions (c–o)	[65]

*p*TosOH = *para*-toluenesulfonic acid; *n*PrCN = *n*-butanenitrile.

Table 13.4 Polymerization of cyclobutanes.




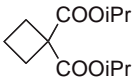

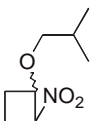
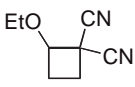
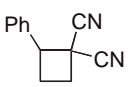
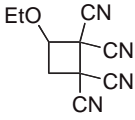
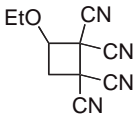
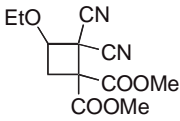
Entry no.	Structure	Experimental conditions	Polymerizability	References
1		Cationic: AlX ₃ /HX (X = Br, Cl), 24–30 °C	Polymerization claimed	[44]
2		Cationic: AlCl ₃ /HCl or Al(OH)Cl ₂ /HCl, 25 °C	Polymerization claimed	[44]
3		Cationic: AlCl ₃ /HCl or AlBr ₃ , 25 °C	Polymerization claimed	[44]
4		Anionic: PhSNa, DMSO	No polymerization	[29]

Table 13.4 Continued

Entry no.	Structure	Experimental conditions	Polymerizability	References
5		Anionic: PhSM (M = Na, K), DMSO, 140–180 °C		[33]
6		Cationic: adventitious electrophilic impurities (triethylamine inhibits the polymerization), 25–35 °C, toluene	Polymerization observed	[66]
7		Anionic: (a) <i>n</i> BuLi, toluene, –78 to –30 °C; (b) NaCN, DMSO, 25 °C; free-radical (AIBN, 60 °C, 10 h)	Polymerizes with anionic initiators; no polymerization under free-radical conditions	[67]
8		Various initiators (<i>n</i> BuLi, toluene, –78 °C or radical initiators); few experimental details	No polymerization	[67]
9		Anionic: (a) THF, RT, various initiators: Et ₃ N, MeONa, <i>t</i> BuOK, MeLi, stable carbanions; (b) EtC(COOEt) ₂ Na, RT, various solvents	Polymerization observed	[68]
10		Free-radical	No polymerization	[68]
11		Spontaneous copolymerization with 2-oxazolines, CH ₃ NO ₂ , RT	Alternating copolymerization by a step-growth mechanism (combination of zwitterions)	[69]

RT = room temperature; DMSO = dimethylsulfoxide.

Table 13.5 Polymerization of [1.1.0]bicyclobutanes.

Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
1		Attempted free-radical copolymerization with acrylonitrile, MMA or SO ₂	Crosslinked materials	[70]
2		Irradiation with UV light	Crosslinked materials	[70]
3		Cationic: BF ₃ ; no experimental details	Oligomers	[70]
4		Free-radical: aqueous copolymerization with acrylonitrile	Crosslinked materials	[70]
5		Free-radical: (a) spontaneous or AIBN or BEt ₃ /O ₂ or K ₂ S ₂ O ₈ , (b) ATRP conditions, CuBr/dNbpy, MBP, 70 °C	Polymerization observed (including living/controlled polymerization; stereochemistry determined)	(a) [70–74]; (b) [4, 75, 76]
		Anionic: (a) NaH, HMPA, (b) <i>t</i> BuMgBr or <i>t</i> BuLi, –95 °C to 0 °C, toluene, (c) <i>t</i> BuLi/EtAl(ODBP) ₂ , –78 °C, toluene	Polymerization observed under some conditions; stereochemistry determined	[70, 72, 77]
6		Free-radical: typical conditions; AIBN, 60 °C	Polymerization observed	[73, 78]
7		Free-radical: typical conditions; AIBN, UV or thermal	Polymerization observed	[73]
	R = ethyl			
	R = –CH _{2cf,3}	Free-radical: typical conditions; AIBN, UV or thermal		
	R = –Ph	Free-radical: typical conditions; AIBN, 60 °C		

Table 13.5 Continued







Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
8	 -COOtBu	Free-radical: AIBN, 60–65 °C, 2-butanone	Polymerization observed	[70]
9	 -CN	Anionic: (a) NaH, HMPA, 0 °C or (b) <i>n</i> BuLi, THF, 0 °C	Polymerization observed; stereochemistry determined	[71, 79]
		Free-radical: (a) thermal (RT), (b) K ₂ S ₂ O ₈ , NaHSO ₃ , (c) AIBN, 50 to 75 °C, (d) (co)polymerization in the presence of ZnCl ₂	Polymerization observed; copolymerization parameters with vinyl monomers and stereochemistry determined; alternating copolymerization with styrene possible	(a–c) [76, 79–85]; (d) [86]
10	 -COOH	Free-radical: AIBN, 50 °C, DMSO	Polymerization observed	[70]
11	 -CONH ₂	Anionic: <i>t</i> BuOK, DMSO, 60 °C	Polymerization observed with anionic rearrangement during the propagation step	[70]
		Free-radical: AIBN, 60 °C, DMSO	Polymerization observed; stereochemistry determined	[71, 70]
12		Free-radical: (a) emulsion recipe, (b) benzoyl peroxide, RT, DMSO, (c) AIBN, DMSO, 50 °C	Polymerization and copolymerization with styrene observed	(a–b) [70]; (c) [76]
13	 -Ph	Free-radical: thermal (25 °C) or peroxide initiators, few experimental details	Polymerization observed: structure not investigated (monomer isomerizes to 1-phenylcyclobutene)	[70, 87]

Table 13.5 Continued

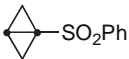
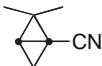
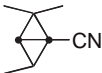
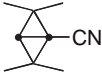
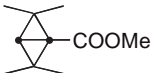
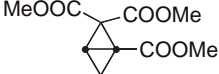
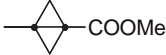
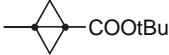




Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
14		Anionic: MeMgBr, <i>n</i> BuLi, <i>t</i> BuOK, no further experimental details	No polymerization	[88]
		Free-radical: AIBN, 65 °C, DMSO	Polymerization observed	[88]
15		Free-radical: AIBN, UV, RT	Polymerization observed	[79, 83]
16		Anionic: <i>n</i> BuLi, THF, RT	Oligomers	[79]
17		Free-radical: AIBN or BPO, 55–60 °C	Polymerization observed with presence of a keteneimine link	[79, 83]
18		Free-radical	Spontaneous polymerization when left at RT	[70]
19		Free-radical: AIBN, 72 °C	Polymerization and copolymerization with vinyl monomers observed	[89]
20		Free-radical: azo initiator, tetramethylene sulfoxide, 75 °C, 6000 atm	Polymerization observed	[70]
21		Free-radical: azo initiator, tetramethylene sulfoxide, 75 °C, 6000 atm	Polymerization observed	[70]
22		Anionic: various anionic initiators, 0–60 °C	Polymerization observed	[79, 90]
23		Free-radical: (a) emulsion recipe or di- <i>t</i> -butyl peroxide; (b) AIBN, 75 °C, CH ₃ CN	Polymerization observed; copolymerization with MMA	(a) [70]; (b) [91]

Table 13.5 Continued

Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
24		Free-radical: AIBN or slurry	Polymerization and copolymerization with styrene observed	[76, 79]
25		Free-radical: AIBN, 60 °C	Polymerization observed	[79]

EtAl(ODBP)₂ = bis(2,6-di-*tert*-butylphenoxy)ethylaluminum; dNbpy = 4,4'-dinonyl-2,2'-bipyridyl; MBP = methyl 2-bromopropionate; AIBN = azo-bis(isobutyronitrile); BPO = benzoyl peroxide; RT = room temperature.

Table 13.6 Polymerization of bicycloalkanes other than [1.1.0]bicyclobutanes.




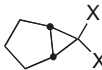
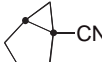
Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
1		Free-radical: conditions not specified	–	[92, 93]
		Anionic: (a) <i>n</i> BuLi in THF or (b) Et ₂ Mg in toluene or (c) MeLi in THF, (a,b,c) –80 to 28 °C	Fast polymerization, polymers not characterized	[92, 93]
2		Free-radical: experimental conditions not specified	–	[92]
		Anionic: Bu ₂ Mg, toluene, –35 °C	Oligomers	[92]
3	 X = H	Coordination/cationic: (a) R ₃ Al/TiCl ₄ , 80–120 °C, (b) BF ₃ gas or BF ₃ ·OEt ₂	Oligomers	[43]
4	 X = Cl	Coordination/cationic: (a) TiCl ₄ or SnCl ₄ or AlCl ₃ , CH ₂ Cl ₂ , –10 to 80 °C, (b) R ₃ Al/SnCl ₄ or TiCl ₄ or WCl ₆ , hexane	Oligomerization; complex structure arising from a rearrangement during the propagation step	[94]
5		Anionic: NaH in tetramethylene sulfoxide	No polymerization	[92, 93]
		Free-radical: (a) emulsion recipe, (b) AIBN or (c) no initiator, 300 °C, 65 kbar	No polymerization except under conditions (c)	[92, 93]

Table 13.6 Continued

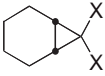
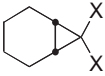





Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
6	 X = H	Coordination/cationic: (a) Ziegler catalyst, (b) $R_3Al/TiCl_4$, 80–120 °C, (c) BF_3 gas or $AlBr_3$, CH_2Cl_2 , –35 to 70 °C	Oligomers	(a) [46]; (b–c) [43]
7	 X = Cl	Coordination/cationic: (a) $TiCl_4$ or $SnCl_4$ or $AlCl_3$, CH_2Cl_2 , –10 to 80 °C, (b) $R_3Al/SnCl_4$ or $TiCl_4$ or WCl_6 , hexane	Oligomerization; complex structure arising from a rearrangement during the propagation step	[94]
8	 X = H	Coordination/cationic: (a) BF_3 , $TiCl_4$ or $SnCl_4$, CH_2Cl_2 , 20–80 °C; (b) $R_3Al/TiCl_4$ or $SnCl_4$ or $VOCl_3$ or WCl_6 , 80 °C; (c) $BF_3 \cdot OEt_2$ or $TiCl_4$ or $SnCl_4$, CH_2Cl_2 , 20–80 °C	Oligomerization; complex structure arising from a rearrangement during the propagation step	(a) [95]; (b–c) [43]
9	 X = Cl	Coordination/cationic: (a) $TiCl_4$ or $SnCl_4$ or $AlCl_3$, CH_2Cl_2 , –10 to 80 °C, (b) $R_3Al/SnCl_4$ or $TiCl_4$ or WCl_6 , hexane	Oligomerization; complex structure arising from a rearrangement during the propagation step	[94]
10	 X = H	Cationic: $VOCl_3$ or $BF_3 \cdot OEt_2$ or $TiCl_4$ or $AlCl_3$, CH_2Cl_2 , 80 °C	Oligomerization; complex structure arising from a rearrangement during the propagation step	[96]
11	 X = Cl	Coordination/cationic: (a) $TiCl_4$ or $SnCl_4$ or $AlCl_3$, CH_2Cl_2 , –10 to 80 °C, (b) $R_3Al/SnCl_4$ or $TiCl_4$ or WCl_6 , hexane	Oligomerization; complex structure arising from a rearrangement during the propagation step	[94]
12	 X = H	Coordination/cationic: (a) BF_3 , $TiCl_4$ or $SnCl_4$, CH_2Cl_2 , 20–80 °C, (b) $R_3Al/TiCl_4$ or $SnCl_4$ or $VOCl_3$ or WCl_6 , 80 °C, (c) $BF_3 \cdot OEt_2$ or $TiCl_4$ or $SnCl_4$, CH_2Cl_2 , 20–80 °C	Oligomerization; complex structure arising from a rearrangement during the propagation step	(a) [95]; (b–c) [43]

Table 13.6 Continued

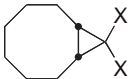
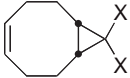


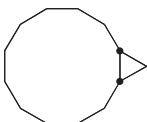
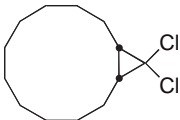
Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
13	 <p>X = Cl</p>	Coordination/cationic: (a) TiCl_4 or SnCl_4 or AlCl_3 , CH_2Cl_2 , -10 to 80°C , (b) $\text{R}_3\text{Al}/\text{SnCl}_4$ or TiCl_4 or WCl_6 , hexane	Oligomerization; complex structure arising from a rearrangement during the propagation step	[94]
14	 <p>X = Cl, Br</p>	Coordination/cationic: $\text{R}_3\text{Al}/\text{TiCl}_4$ or SnCl_4 or WCl_6 or ZrCl_4 or RhCl_3 , 0 – 70°C	Oligomerization, complex transannular rearrangement mechanism involving the $\text{C}=\text{C}$ bond during the propagation step	[97]
15	 <p>X = H</p>	Cationic: VOCl_3 or $\text{BF}_3 \cdot \text{OEt}_2$ or TiCl_4 or AlCl_3 , CH_2Cl_2 , 80°C	Oligomerization; complex structure arising from a rearrangement during the propagation step	[96]
16	 <p>X = Cl</p>	Coordination/cationic: (a) TiCl_4 or SnCl_4 or AlCl_3 , CH_2Cl_2 , -10 to 80°C , (b) $\text{R}_3\text{Al}/\text{SnCl}_4$ or TiCl_4 or WCl_6 , hexane	Oligomerization; complex structure arising from a rearrangement during the propagation step	[94]
17		Coordination/cationic: (a) BF_3 , TiCl_4 or SnCl_4 , CH_2Cl_2 , 20 – 80°C , (b) $\text{R}_3\text{Al}/\text{TiCl}_4$ or SnCl_4 or VOCl_3 or WCl_6 , 80°C , (c) $\text{BF}_3 \cdot \text{OEt}_2$ or TiCl_4 or SnCl_4 , CH_2Cl_2 , 20 – 50°C	Oligomerization; complex structure arising from a rearrangement during the propagation step	(a) [95]; (b–c) [43]
18		Cationic: AlCl_3 or TiCl_4 or SnCl_4 , CH_2Cl_2 , 50 – 80°C	Oligomerization; complex structure arising from a rearrangement during the propagation step	[98]

Table 13.6 Continued

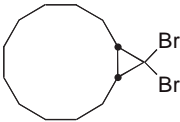
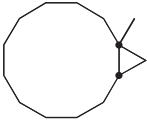
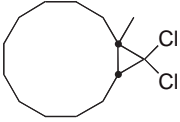
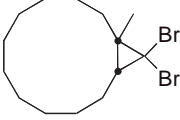
Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
19		Cationic: AlCl_3 or TiCl_4 or SnCl_4 , CH_2Cl_2 , 50–80 °C	Oligomerization; complex structure arising from a rearrangement during the propagation step	[98]
20		Cationic: VOCl_3 or $\text{BF}_3 \cdot \text{OEt}_2$ or TiCl_4 or AlCl_3 , CH_2Cl_2 , 80 °C	Oligomerization; complex structure arising from a rearrangement during the propagation step	[96]
21		Cationic: AlCl_3 or TiCl_4 or SnCl_4 , CH_2Cl_2 , 50–80 °C	Oligomerization; complex structure arising from a rearrangement during the propagation step	[98]
22		Cationic: AlCl_3 or TiCl_4 or SnCl_4 , CH_2Cl_2 , 50–80 °C	Oligomerization; complex structure arising from a rearrangement during the propagation step	[98]

Table 13.7 Polymerization of other highly strained polycycloalkanes (propellanes, dehydroadamantanes, etc.).

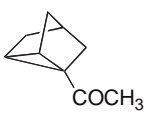
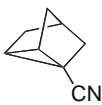
Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
1		No description of experimental conditions provided (note in a review paper)	No polymerization	Page 385 in [99]
2		No description of experimental conditions provided (note in a review paper)	No polymerization	Page 385 in [99]

Table 13.7 Continued





Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
3		Free-radical/spontaneous: (a) thermal, (b) benzoyl peroxide, irradiation, (c) thermal, RT, vinyl comonomer, (d) polymerization in ZMS-5 zeolite	(Co)polymerization observed; alternating copolymerization with maleic anhydride	(a) [100–103]; (a–b) [104–106]; (b) [107]; (c) [108, 109]; (d) p. 227 in [16] (unpublished results)
4		Anionic: <i>n</i> BuLi, few experimental details	Oligomerization	[100, 101, 104, 106]
5	 R = <i>n</i> -pentyl	Cationic: adventitious electrophilic impurities	Polymerization observed	[110, 111]
6	 R = <i>n</i> -pentyl	Free-radical: thermal, RT, Et ₂ O, vinyl comonomer, (b) AIBN, propellane comonomer	Copolymerization observed	(a) [112]; (b) [111]
7	R = <i>n</i> -hexyl	Cationic: adventitious electrophilic impurities	Polymerization observed	[110]
8	R = <i>n</i> -undecyl	Cationic: adventitious electrophilic impurities	Polymerization observed	[110]
9	R = -(CH ₂) ₃ OCH ₃	Cationic: adventitious electrophilic impurities	Polymerization observed	[110, 113]
10	R = -(CH ₂) ₅ OCH ₃	Cationic: adventitious electrophilic impurities	Polymerization observed	[110]
11	R = -(CH ₂) ₂ O(CH ₂)OCH ₃	Free-radical: AIBN, UV irradiation, RT	(Co)polymerization observed	[111, 114]
12	R = -CH ₂ OSiMe ₂ tBu	Free-radical: (a) AIBN, (meth)acrylate comonomer; (c) thermal, (meth)acrylate comonomer	Copolymerization observed	[115]

Table 13.7 Continued



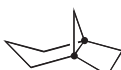



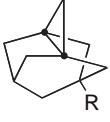



Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
13		Anionic: tBuLi or PhLi, hexane, 20°C	Polymerization observed	[116, 117]
14		Free-radical: thermal, RT, acrylonitrile	Alternating copolymerization with acrylonitrile observed	[118, 119]
15		Free-radical: (a) thermal, RT, (b) thermal reaction with oxygen	Polymerization observed, alternating copolymerization with O ₂	(a) [120]; (b) [121]
16	 R = H	Free-radical: (a) thermal (140–160°C), (b) bulk, no initiator, 80°C, (c) AIBN	polymerization and alternating copolymerization with O ₂ observed	(a) [122, 123]; (b–c) [124]
17	 R = <i>n</i> -Bu	Free-radical: (a) bulk, no initiator, 80°C, (b) AIBN	Polymerization observed	[124]
18	 R = Br	Unknown mechanism: (thermal, >120°C)	Polymerization suggested	[125]
19	 R = H, <i>n</i> Bu	Cationic: CF ₃ SO ₃ H, CH ₂ Cl ₂ , 0°C	Polymerization observed	[124, 126]

Table 13.7 Continued

Entry no.	Structure	Experimental conditions	Polymerizability	Reference(s)
20	 <p>R = H, nBu</p>	Anionic: <i>n</i> BuLi or PhMgBr, THF, RT	No polymerization	[124]
21		Free-radical: thermal, 145 °C, overnight	Polymerization observed	[122]
22		Cationic: AlCl ₃ , CS ₂ , 20 °C	Oligomers	[127]

AIBN = azo-bis(isobutyronitrile); RT = room temperature.

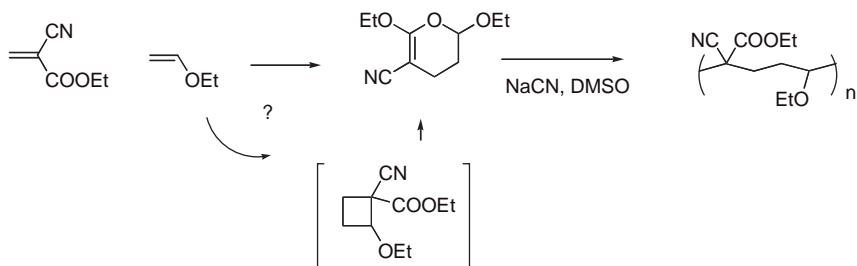
13.3.1

The Polymerization of Monocyclic Alkanes

13.3.1.1 Cyclopropane Rings

The only claim for a free-radical ROP involving a cyclopropane [17, 63, 64] was later proved to be wrong [18] and, to the best of our knowledge, no convincing evidence has ever been provided that a cyclopropyl ring can be opened by a free radical. Yet, nucleophilic and electrophilic ring opening are possible, and corresponding ROPs have been observed accordingly.

Cationic polymerizations often suffer from the ability of carbocations to easily rearrange and lead to side reactions. This is particularly true in the case of cyclopropane ROPs, as the propagation steps in this case are slow reactions, much slower than for vinyl cationic propagations. As a result, rearrangements become competitive with propagation, and lower the polymerization efficiencies via transfer reactions. In some cases—but not always—rearranged carbocations are still capable of propagating, and several units (rearranged and ‘normal’) become part of the final polymer structures. Consequently, cationic ROPs of cyclopropanes have most often yielded oligomers of low molecular weights and complex structures. It must be emphasized that most experimental results in this area date back from the 1950s and 1960s—well before strategies were introduced by polymer chemists to effectively control cationic polymerizations. In this context, it would be interesting to examine whether some of these controlled techniques might be able to overcome these practical limitations. Also noteworthy here is the fact that



Scheme 13.3

many of the monomers investigated thus far are only weakly activated by the substituent(s) introduced on the cycle (alkyl groups, halogens). One might wonder whether more activating substituents such as ethers might not lead to more efficient polymerization reactions.

The anionic polymerization of cyclopropanes has been more successful, with several examples of ‘living’ polymerizations having been reported [27, 33]. Here also, activation by side groups plays a key role. As a rule of thumb, two electron-withdrawing substituents on the same carbon are often needed for the polymerization to be efficient, but even with this array of activating groups, these cyclopropanes are still drastically less reactive than the corresponding vinyl monomers [as shown for example by the relative polymerizabilities of a cyclopropane geminally substituted by a nitrile and an ester versus the corresponding α -cyanoacrylate (‘super-glue’)] [33]. Electron-donating groups (or other substituents capable of stabilizing a partial positive charge) can be added on the vicinal carbon to further increase the reactivity, but unfavorable steric interactions with the approaching propagating center can partly overcome the gained benefit. This approach is also somewhat limited by the tendency observed for these ‘hyperactivated’ monomers to rearrange to less-strained structures before a polymerization could take place (see, for example, Ref. [128]). In some rare cases (see Scheme 13.3 for an example), a polymerization of the rearranged structure can be observed, leading to a polymer whose final structure corresponds to the one expected—had the ROP of the ‘phantom’ cyclopropyl monomer been possible [129, 130].

In addition to the cyclopropanes described above whose polymerizability is easy to reconcile with the traditional reactivity schemes of organic chemistry, one monomer described by Soga *et al.* in 1978 (entry 2 in Table 13.3) displays a very peculiar behavior [65]. Substituted by one ester group on every carbon of the three-membered ring, it does not polymerize with any initiator other than hydrobromic acid. Spectroscopic evidences are consistent with a simple $((\text{CHCOOR})_3)_n$ linear structure.

13.3.1.2 Cyclobutane Rings

Despite strain energies similar to cyclopropanes, cyclobutanes display a much lower tendency to ring-open, a trend also observed in three- versus four-membered heterocyclic rings. Reasonable evidences for a ROP have only been reported in highly activated systems (see Table 13.4). Typical examples include the

anionic polymerization of cyclobutanes substituted by two nitrile groups on one carbon, and further substituted by a phenyl or an ether group on the neighboring carbon (examples 6–11 in Table 13.4). This substitution pattern imparts polarization to the C–C bond and assists in the heterolytic cleavage when a nucleophile attacks on the carbon substituted by the ether. It must be mentioned that, except for the spectroscopic evidences that the polymer structure results undeniably from a ROP, very few additional data are provided in the original contributions (such as M_n , end-groups or tacticity of the formed polymers).

13.3.2

The Polymerization of Polycyclic Rings

Among polycyclic rings, [1.1.0]bicyclobutanes (see Table 13.5) deserve a special place due to the extensive amount of work reported in the literature. Reviews specifically addressing the polymerization of these monomers are available [7–9]. Free-radical, anionic and, in some rare cases, cationic polymerizations have been observed, and the influence of a large variety of substituents on the polymerizability investigated. Substituents placed on the carbons of the bond to be cleaved (indicated by heavy dots in Table 13.5) include alkyl, aryl and allyl groups, electron-withdrawing substituents (carboxylic acid and esters, nitrile, carboxamide, ketone and sulfone). Anionic polymerizations have been observed when the bicyclobutane is activated by an ester, a nitrile or a carboxamide. In the latter case, an intramolecular rearrangement of the $-\dot{C}-(C=O)-NH_2$ propagating carbanion to a $-\dot{CH}-(C=O)-NH^-$ N-centered anion occurs in analogy to acrylamide anionic polymerization [70]. The stereochemistry has been determined in some cases, although no example of a perfectly stereoregular polymers has been described thus far [80–77]. The reactivity under free-radical polymerizations conditions is generally good and reminiscent of the polymerizability displayed by vinyl monomers. As a result, a ‘living’/controlled free-radical polymerization via an atom transfer radical polymerization (ATRP) mechanism has been described for methyl 1-bicyclobutane carboxylate, providing decently narrow molecular weight distributions and adequate control of the molecular weights [4, 75]. An A–B polystyrene diblock copolymer was also obtained by the same authors, using the bromo-terminated poly(bicyclobutanecarboxylate) as a macroinitiator. Bicyclo[$n.1.0$]alkanes with $n > 1$ have also been polymerized (Table 13.6).

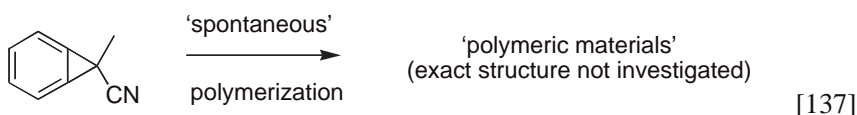
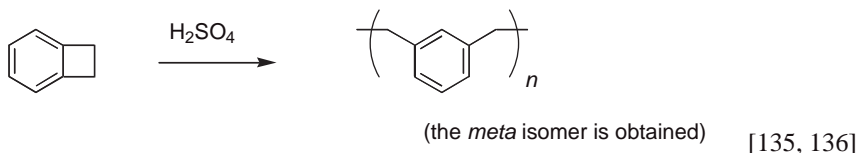
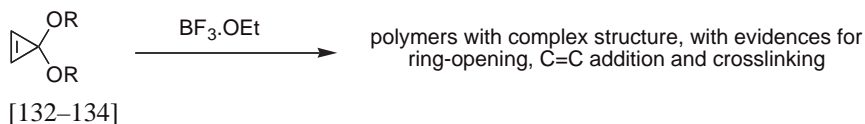
Other strained structures include propellanes – molecules with two vicinal carbons independently connected by three separate bridges. These compounds exhibit an inverted tetrahedron at the bridge carbons, and are so reactive [21, 131] that they polymerize ‘spontaneously’ or in the presence of trace impurities (see Table 13.7).

13.3.3

Unusual Examples

In the absence of a detailed mechanistic investigation, a few examples available in the literature are difficult to categorize according to the format used in this chapter.

Formally, the affected monomers and obtained polymers match the definition of a cycloalkane direct ROP, but the known chemistry of the monomers or close analogues casts some doubts on the polymerization mechanism. Of specific concern are monomers known to rearrange into molecules whose polymerization becomes possible via an addition on a C=C double bond. A few examples are presented below:



13.4

Summary and Prospects

As outlined in this chapter, polymerizable cycloalkanes can be roughly divided into two families: (i) highly strained, polycyclic molecules with high intrinsic polymerizabilities (e.g. bicyclo[*n*.1.0]bicycloalkanes and [*m.n*.1]propellanes); and (ii) monocyclic cycloalkanes, mostly cyclopropanes with a few cyclobutanes, that require further activation by judiciously placed substituents.

Both groups display specific scope and limitations. The high reactivity of the first class of monomers in chain polymerization—equal or superior to vinyl monomers—represents a considerable asset, but the difficulty and cost of synthesizing and storing them severely limits their use. The second class of monomers is often easier to synthesize, with a few members being available commercially. The indispensable activating substituents can be either useful or detrimental, depending on the considered applications. More restrictive is the low rate of propagation displayed by these monomers that require specific mechanistic studies and optimization of polymerization conditions in order to obtain acceptable degrees of polymerization. Finally, high symmetry in the obtained polymers and/or the presence of polar substituents often induce, in both families, a high tendency to crystallize, low tractabilities and poor solubilities in usual solvents. This solubility limitation can sometimes be overcome by adding specific pendant groups [27, 31, 110, 112].

Research in this area has long been driven by the ambition of discovering new, potentially useful monomers to add to the pool of structures available to polymer

chemists, and by a desire to expand our understanding of structure–property relationships in organic polymer chemistry. During the past 10–15 years, it appears that this trend has partly shifted. Most recent reports have concentrated to a large extent on the properties of the polymers/oligomers (better thermal stabilities, piezoelectric properties, etc.) and/or on the prospect of exploiting the original structural/geometrical features offered by the polymer backbone (rigidity, longer distances between neighboring groups, etc.) in nanotechnology. Whether the current set of available monomers is appropriate to reach these objectives or will require additional structures, might be the key question whose answer will decide the fate and future direction of this field of research.

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14

Metal-Free Catalysis in Ring-Opening Polymerization

Andrew P. Dove

14.1

Introduction

In recent years, the application of metal-free strategies to mediate ring-opening polymerization (ROP) reactions has developed into an important aspect of the field. Metal-free strategies for the synthesis of polymers provide several advantages over those that require metals to mediate the process, the most obvious being the absence of the costly removal of metal impurities from the resultant polymers. Many of these systems also offer enhanced stability to trace impurities such as water and oxygen, making the preparation and storage of catalysts extremely simple. Of course, in addition to metal-based and ‘organocatalytic’-mediated polymerization, larger metal-free compounds—namely enzymes—have also shown significant promise in the area of ROP (this subject is covered in Chapter 15). In this chapter we will primarily focus on the ROP of cyclic esters, although mention of other important advances in the field of metal-free ROP of other monomers will be made as appropriate.

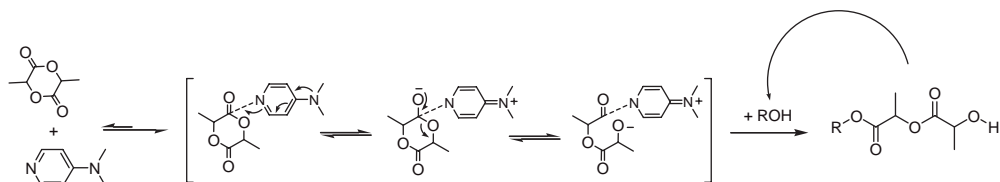
14.2

Nucleophilic ROP

14.2.1

Tertiary Amines and Phosphines

Amongst the simplest metal-free catalysts are tertiary amines and phosphines. In 2001, Hedrick and coworkers reported the ROP of lactide using 4-(dimethylamino)pyridine (DMAP) and 4-pyrrolidinopyridine (PPY) [1]. The polymerization of either D,L- or L-lactide was shown to proceed in a ‘living’ manner in both dichloromethane (DCM) at 35 °C and in the melt at 135 and 185 °C, respectively. DMAP was shown to be highly effective even at very low catalyst loadings (0.1 equiv. relative to the initiating alcohol), although at lower loadings and



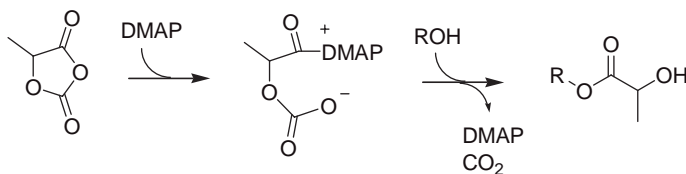
Scheme 14.1 Proposed mechanism for the ROP of lactide by DMAP. (Reprinted from Ref [1].)

temperatures the conversion was slow. The correlation between molecular weight and conversion was found to be consistent with that of a ‘living’ polymerization and the polydispersity index (PDI) remained low throughout the polymerization. Furthermore, it was found that, in contrast to many organometallic-promoted polymerizations, the PDI was invariant to high monomer conversions, which is indicative of any transesterification side reactions being undetectable. At higher temperatures (melt conditions), high conversions could be obtained in about 5–20 min, depending on the target degree of polymerization (DP) with the control over polymerization remaining high. Commercially available DMAP, immobilized on a solid support, was also shown to be an effective catalyst for the ROP of lactide. This polymerization was proposed to proceed via a monomer-activated mechanism in which a nucleophilic attack of amine onto the lactide monomer resulted in a zwitterionic species that was susceptible to attack by the initiating or propagating alcohol chain-end (Scheme 14.1).

By taking advantage of the ability of DMAP to efficiently catalyze transesterification reactions, Hedrick and colleagues also demonstrated the ability to control the molecular weight of poly(lactic acid)s (PLAs) by a chain scission/depolymerization methodology [2]. In this study, PLAs of various molecular weights were allowed to react in DCM solution at 36 °C, or in bulk at either 135 and 185 °C in the presence of various compositions of benzyl alcohol, together with 2.5 equiv. of DMAP or PPY, with a systematic and controlled decrease in molecular weight being demonstrated. This methodology was also used to prepare star polymers by use of a pentaerythritol and block copolymers by applying monohydroxy functional poly(ethyleneoxide) (PEO) oligomers. Interestingly, the presence of excess primary or secondary alcohol resulted in the quantitative conversion to the monoester and diester products, respectively.

The application of DMAP as a catalyst for the ROP of lactide has been exploited in the synthesis of hyperbranched poly(D-mannan)-*b*-poly(lactic acid) [3] and poly(lactic acid)-*b*-dendritic poly(L-lysine) [4] block copolymers, as well as in the synthesis of functional/substituted poly(glycolic acids) [5]. DMAP was shown recently also to catalyze the ROP of ϵ -caprolactone in the synthesis of a chitosan-*graft*-poly(ϵ -caprolactone) [6].

In a subsequent study, Hedrick and coworkers demonstrated that nucleophilic phosphines were also able to act as highly efficient ROP catalysts [7]. In this example, it was necessary to perform the polymerizations in bulk at high temperature, whereupon the catalyst concentration was found to have a significant effect on the control of the polymerization, with >1 equiv. (relative to initiator) resulting



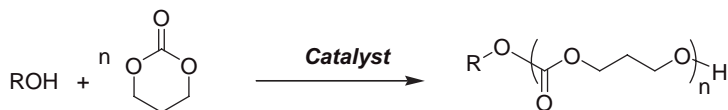
Scheme 14.2 ROP of OCA by DMAP. (Adapted from Ref. [8].)

in broadened polydispersities, indicative of adverse transesterification. However, the application of 1 equiv. $P(n\text{-Bu})_3$, $P^t\text{(Bu)}_3$, PhPMe_2 , Ph_2PMe or PPh_3 resulted in well-controlled polymerizations with the most basic/nucleophilic phosphines being the most highly active ROP catalysts. A comparable monomer-activated ROP mechanism to that of the tertiary amines was proposed for this catalyst.

Recently, Bourissou and coworkers showed that the ROP of 1,3-dioxolane-2,4-diones (*O*-carboxyanhydrides, OCAs) catalyzed by DMAP provided an excellent alternative method for the synthesis of PLA [8]. The ROP of the lactic acid–OCA (L-lacOCA) revealed that complete conversion of the OCA occurred in 5 min at room temperature, at a monomer: initiator: catalyst ratio of 20:1:1. In this way, well-controlled PLAs could be synthesized with good control and displaying a linear increase of molecular weight with monomer conversion to produce polymers with narrow polydispersities (<1.22). The ‘living’ character of the polymerization was further confirmed by demonstration of the end-group fidelity of the polymers, and the finding that polymerization could be reinitiated by the addition of a second batch of monomer to a polymerization experiment. Polymerization was proposed to occur via monomer activation by nucleophilic attack of DMAP at the most electrophilic carbonyl group of lacOCA, followed by esterification with the initiating/propagating alcohol and concurrent loss of carbon dioxide (Scheme 14.2). This liberation of a gaseous byproduct provides a considerable driving force for the reaction.

The application of cyclic anhydrides for polymer synthesis using metal-free strategies is not limited to OCAs [9, 10]. In 2004, Hadjichristidis and colleagues reported that α -amino acid *N*-carboxyanhydrides (NCAs) could be efficiently polymerized in the absence of any catalyst species, the basicity of the initiating/propagating amine being sufficient to result in a controlled ROP [9]. In this example, an extremely rigorous high-vacuum/air-sensitive methodology was required to prevent contamination of the system from trace impurities that may lead to a loss of control over the polymerization. The NCA monomers could be successfully polymerized in dimethylformamide (DMF) solution at ambient temperature to produce polypeptides of predictable molecular weight and with narrow polydispersities (1.02–1.16) exclusively by the ‘normal-amine’ route. Kricheldorf, Lomadze and Schwarz have also demonstrated the ROP of dithiolane-2,4-diones to synthesize poly(thioglycolide) and poly(thiolactide) [10]. Polymerization was shown to occur both thermally and catalyzed by pyridine or triethylamine.

The ROP of cyclic carbonates such as trimethylene carbonate (TMC) to synthesize poly(carbonate)s (Scheme 14.3) has also been shown to be mediated by



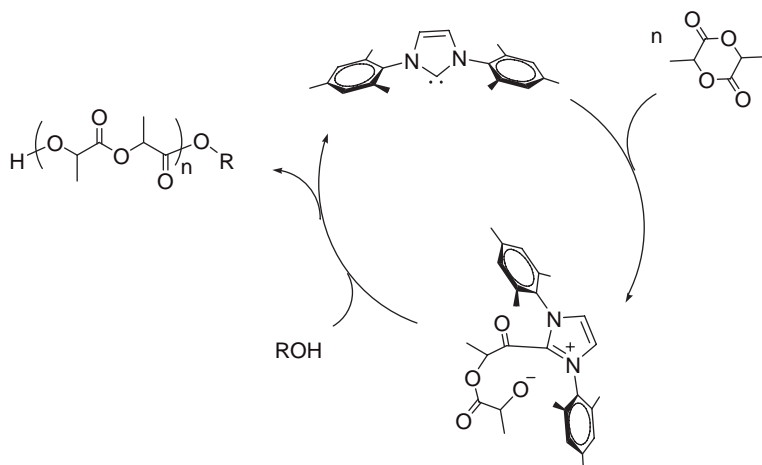
Scheme 14.3 ROP of trimethylene carbonate (TMC).

nucleophilic bases. Endo and colleagues found that the ROP of TMC and 2,2-dimethyltrimethylene carbonate (DTC) could be effectively performed without a catalyst present, propagating by a nucleophilic attack of the propagating species on the monomer [11, 12]. The ROP, under strictly anhydrous conditions in the melt at 150 °C or 120 °C, produced polymers with molecular weights which corresponded well with those predicted from the monomer: initiator ratio, albeit with rather broad polydispersities (1.51–1.97). These methods were applied to the synthesis of linear and star-shaped poly(ethylene glycol) (PEG) block copolymers. Bowden and coworkers reported that a tertiary amine-functionalized initiator, 2-(dimethylamino)ethanol (DMAE) resulted in an efficient ROP of TMC, slightly above the monomer melting point (50 °C) [13]. Under these conditions a controlled polymerization was observed that displayed a linear increase of M_n with monomer conversion producing polymers (target DP 40) within 6 h and with PDIs of approximately 1.30. Application of the benzoic acid ester of DMAE also resulted in an efficient ROP.

14.2.2

N-Heterocyclic Carbenes

Over recent years, significant interest has been taken in the application of *N*-heterocyclic carbenes (NHCs), and consequently these compounds have emerged as powerful nucleophiles, leading to their application as organic catalysts [14–16]. Among these roles, NHCs have proved to be extremely powerful catalysts for the ROP of cyclic esters (among other monomers). In 2002, Hedrick and coworkers reported the first example of NHCs as catalysts for the ‘living’ polymerization of cyclic esters [17]. In this study 1,3-bis-(2,4,6-trimethylphenyl)imidazol-2-ylidene (IMes) was applied as a catalyst for the ROP of lactide, ϵ -caprolactone and β -butyrolactone, and in each case polymerization was shown to proceed efficiently, producing polymers of predictable molecular weight (based on monomer: initiator ratio) and narrow polydispersity with high end-group fidelity. In the case of lactide, a linear increase in molecular weight with monomer conversion was also demonstrated, with PLAs of molecular weight in excess of 25 000 g mol⁻¹ being reported to be synthesized within 10 min. Further studies have shown that PLAs with a DP of 100 can be obtained in about 1 min [14]. The polymerizations displayed no solvent dependency, and highly controlled polymerization was possible even at very low catalyst concentrations (i.e. 1:80:1200, catalyst: initiator: monomer). The rate of polymerization was shown to be highly dependent on the electronic nature of the carbene substituents, with more electron-withdrawing backbone substituents displaying markedly lower reactivities towards ROP [18].

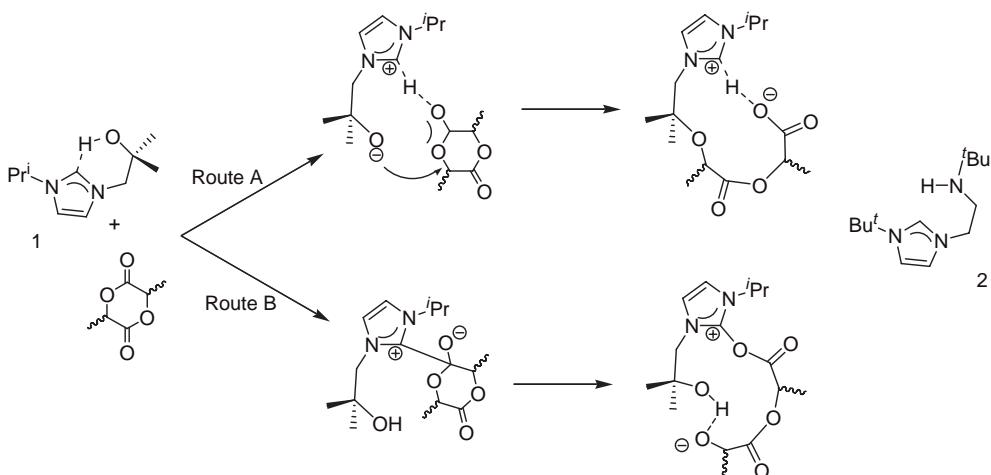


Scheme 14.4 Proposed 'monomer-activated' mechanism for the ROP of lactide by IMes. (Adapted from Ref. [14].)

A study of the ROP of D,L-lactide catalyzed by the IMes carbene revealed a preference for isotactic enchainment, such that conducting the polymerization at -20°C resulted in a PLA with a probability of isotactic enchainment (P_m) of 0.75 [19]. Further studies revealed that, at -70°C , the P_m could be increased to 0.83 [20]. The application of a more sterically hindered carbene at -70°C further enhanced the isotacticity of the polymer to $P_m = 0.90$. Interestingly, the application of sterically hindered chiral carbenes did not further enhance the stereocontrol of the ROP process, which suggested that a chain-end-controlled process was dominating the stereoselectivity.

A monomer-activated mechanism was proposed in which the monomer was subject to a nucleophilic attack by the NHC to form a carbene–monomer zwitterionic adduct that initiated/propagated by esterification with the initiating alcohol or propagating chain-end, respectively (Scheme 14.4) [17]. Recent data provided by Arnold and coworkers showed that the addition of 1 equiv. of D,L-lactide to a bifunctional NHC-tertiary alcohol, **1**, in tetrahydrofuran (THF), pyridine or toluene, and the absence of an additional alcohol initiator, resulted in a mixture of two products: (i) the coordination–insertion product, in which **1** behaves as an alkoxide initiator (Scheme 14.5, route A); and (ii) the carbene attack product, in which **1** behaves as a nucleophile (Scheme 14.5, route B) [21]. Interestingly, the application of an analogous NHC-secondary amine (**2**) only resulted in identification of the NHC nucleophilic attack product forming polymers with an imidazolium chain-end, as determined by matrix-assisted laser desorption ionization (MALDI) mass spectrometry, and providing compelling support for the original proposed mechanism.

In the absence of protic initiators, Waymouth and coworkers showed that it is possible to synthesize cyclic polymers [22, 23]. In THF solution, the ROP of lactide was shown to produce cyclic polymers with PDI <1.3 (less than 90% monomer

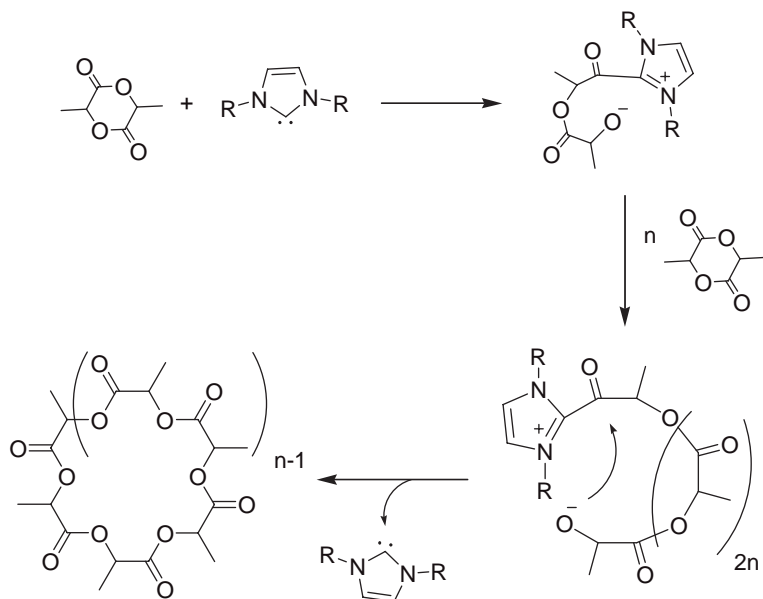


Scheme 14.5 Ring-opening of lactide by functional NHCs. (Adapted from Ref. [21].)

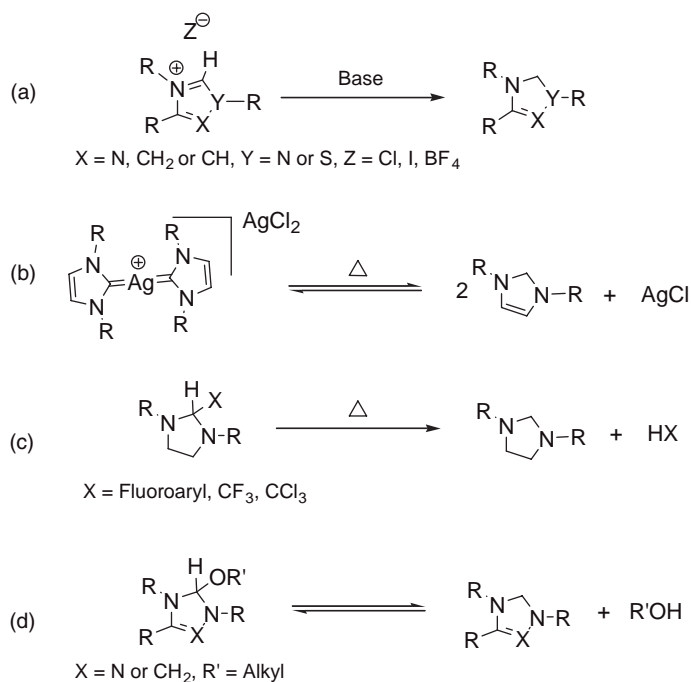
conversion) with a linear increase of molecular weight with monomer conversion [22]. The cyclic structure was confirmed by matrix-assisted laser desorption ionization time-of-flight (MALDI-ToF) mass spectrometry, in addition to viscosity and light-scattering measurements. However, the MALDI-ToF studies revealed that the peaks were separated by 72 mass units (corresponding to half the mass of a lactide unit), indicating that transesterification had taken place during the polymerization reaction. Kinetic studies were consistent with a polymerization in which the rate of propagation was greater than the rate of initiation, resulting in higher molecular weights at low conversions than would be expected from the monomer:initiator ratio. These authors proposed a zwitterionic mechanism in which initiation occurred by attack of the NHC on lactide, with propagation occurring by ring expansion (Scheme 14.6).

Further studies conducted by Jeong, Hedrick and Waymouth showed that the application of 1,3-dimesitylimidazolin-2-ylidene efficiently mediated the ROP of β -butyrolactone and β -propiolactone to form cyclic polymers, and with good control over the molecular weight and polydispersities <1.3 [23]. A kinetic analysis showed the ROP to be first order with respect to both monomer and carbene concentrations. The integrity of the initiation step was confirmed by the isolation of the spiro imidazolidine compound formed by the equimolar reaction of β -butyrolactone and carbene.

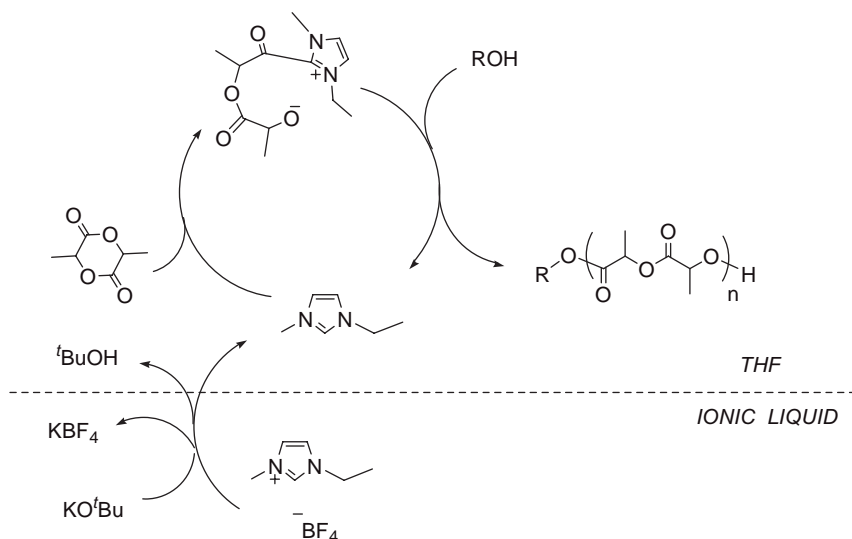
A large number of investigations have focused on the *in situ* generation of NHCs from air-stable precursors [18, 24–28]. The most simple of these approaches is the liberation of free NHCs from their respective acid salts (Scheme 14.7a), thereby enabling a straightforward examination of the effect of NHC structure on polymerization behavior [18]. A wide range of imidazolium, imidazolinium and thiazolium compounds were evaluated as precatalysts for the ROP of lactide and other cyclic esters. The *in situ* generation of the corresponding carbene compound was achieved by reaction with either potassium *tert*-butoxide or triethylamine, and



Scheme 14.6 Proposed synthesis of cyclic poly(lactide) by zwitterionic ROP. (Adapted from Ref. [22].)



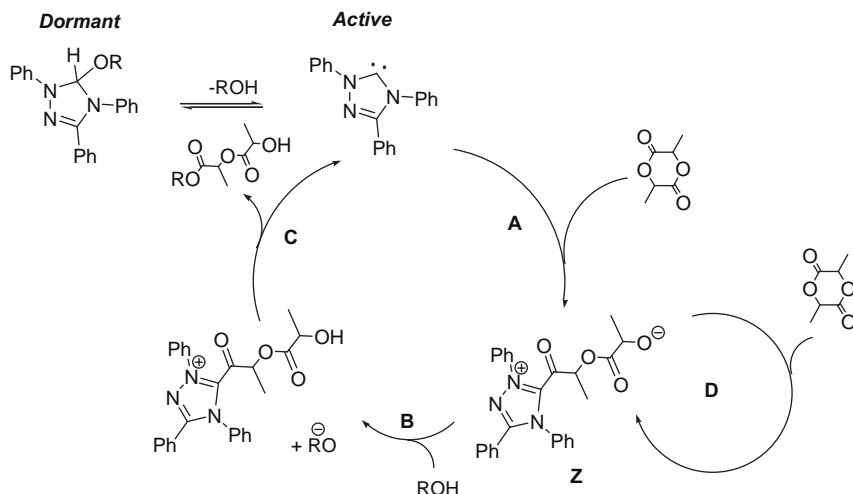
Scheme 14.7 *In situ* generation of NHCs. (Adapted from Ref. [16].)



Scheme 14.8 ROP of lactide using an ionic liquid catalyst reservoir. (Adapted from Ref [14].)

showed all catalysts to promote efficient and well-controlled ROP of lactide, with the imidazolium- and imidazolinium-derived catalysts displaying much higher activity than their thiazolium-derived analogues. Furthermore, solid-supported catalysts were applied and shown to be highly effective ROP catalysts.

This methodology was extended to generate free carbene catalyst from a system in which an ionic liquid (IL) was able to act as a catalyst reservoir (Scheme 14.8) [18]. Both, a homogeneous system and a biphasic system that was comprised of THF and the IL were shown to provide an efficient generation of free carbene *in situ* upon the addition of potassium *tert*-butoxide. Polymerization in neat IL resulted in the precipitation of PLA when a DP of approximately 150 had been achieved, whereas the biphasic system enabled higher-molecular-weight PLAs to be synthesized. Furthermore, the authors showed that recycling of the catalyst reservoir was possible. Other one-pot routes examined the release of free carbenes from their corresponding silver salts (Scheme 14.7b) [27] and thermal generation from electron-withdrawing aryl adducts that could be synthesized directly from the corresponding diamine and substituted benzaldehyde (Scheme 14.7c) [24]. A further development of this strategy led to the discovery of one-component catalyst/initiator alcohol adducts (Scheme 14.7d) [25, 26, 28]. These compounds are accessible either by reaction of the free carbene and the corresponding alcohol, or by liberation of the imidazolinium salt with an appropriate alkali metal alkoxide (they are often also generated *in situ* by reaction of potassium hydride and alcohol). The adducts were shown to reversibly eliminate alcohol at ambient temperature, with the resultant solutions capable of mediating the ‘living’ polymerization of lactide which had been initiated by the alcohol generated *in situ*. This approach has enabled the simple synthesis of storable and stable multifunctional- and macroinitiators for ROP.



Scheme 14.9 Proposed mechanism for ROP of lactide by triazole carbene. (Adapted from Ref. [28].)

This methodology has been extended to the more thermally stable alcohol adducts of the commercially available 1,3,4-triphenyl-4,5-dihydro-1*H*-1,2-triazol-5-ylidene. Dubois, Hedrick, Waymouth and coworkers showed that the polymerization of L-lactide in toluene at 90 °C (target DP = 70) proceeded to near-quantitative conversion within 50 h, producing a polymer with excellent molecular weight and end-group control [25]. Although polymerization did occur at lower temperatures, the ROP was extremely slow and produced polymers with broad or multimodal distributions. The strong adduct which formed at room temperature enabled a reversible termination of ROP to take place by simply modulating the temperature of the reaction. Furthermore, the low activity of the system effectively eliminated transesterification side reactions at low temperature.

Kinetic analysis of the polymerization revealed a first-order dependence on monomer, triazole carbene and alcohol when [triazole]/[alcohol] = 1, operating by a mechanism comparable to that proposed previously (Scheme 14.9). However, altering the ratio of triazole to alcohol such that [triazole]/[alcohol] > 1 resulted in the observation of a nonlinear dependence of rate on [triazole], and suggesting that a second pathway for lactide enchainment had become significant [28]. The authors proposed that, at high [triazole]/[alcohol] ratios, the direct addition of lactide to the zwitterionic intermediate **Z** (Scheme 14.9, path D) was able to compete with proton transfer (Scheme 14.9, path B). Further confirmation of the presence of competing mechanisms was obtained by analysis of an unquenched polymerization sample by electrospray ionization mass spectrometry (ESI-MS), in which the primary peaks were attributed to triazole end-capped polymers, while minor peaks were observed for both hydroxyl-terminated and macrocyclic PLAs.

This catalyst system was also applied to the synthesis of a wide range of functional, block and dendritic star copolymers [25, 28]. Further investigations into the

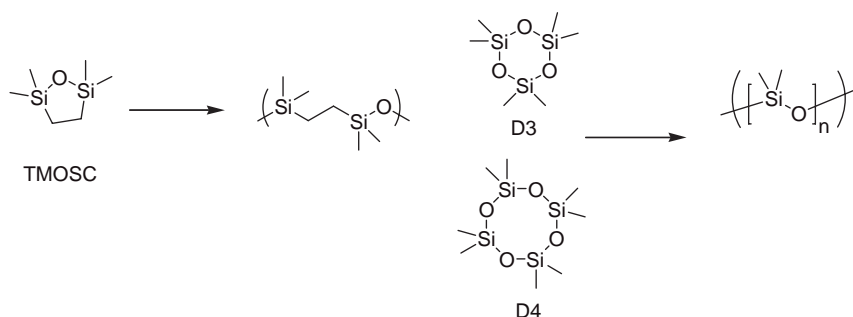
applicability of this system for the polymerization of lactide revealed that application of primary amine initiators led directly to multifunctional polymers [29]. Examination of the methine end groups in comparison to the initiating group revealed two end groups per initiating group, suggesting that initiation from both N–H groups of the primary amine was occurring. Polymerization initiated from ϵ -caprolactam confirmed that initiation was indeed possible and quantitative from an amide, and the technique was extended to produce more complex H- and super-H-shaped polymer architectures from simple primary amine-functionalized initiators.

Triazole carbenes have also proved to be highly efficient catalysts for the ROP of β -lactones [28, 30]. The polymerization of β -butyrolactone, initiated by methanol in the presence of the triazole catalyst at 80°C in toluene, resulted in polymerization in which both O-acyl and O-alkyl ring-opening was occurring, as indicated by the presence of both α -methoxy and crotonate end groups by ^1H NMR analysis. However, the addition of *tert*-butyl alcohol as a cosolvent to favor formation of the alcohol adduct and minimize the concentration of free triazole (*tert*-butyl alcohol cannot initiate the polymerization) effectively eliminated the presence of crotonate-initiated polymer chains below DP 200. In this system, the ROP proceeds in a well-controlled manner, with molecular weights matching those predicted by the monomer: initiator ratio, low polydispersities, high end-group fidelity and a linear increase of molecular weight with monomer conversion. Attempts to synthesize higher-molecular-weight polymers (DP 250–450) tended to show some broadening of polydispersity, accompanied by the observation of a small amount of crotonate end-capped polymer (~25% of total chain ends). When Dubois and coworkers applied an extension of these techniques to the ROP of dimethyl benzyl β -malolactonate, the homopolymerizations proceeded very slowly and as such the copolymerization of this monomer with β -butyrolactone was investigated. The polymerization was shown to proceed with complete end-group fidelity and excellent control over the polymer molecular weights and dispersities.

In a related study, Hedrick, Waymouth and coworkers reported that NHCs were also able to act as catalysts for the ROP of trimethylene carbonate (target DP 50) [31]. The application of 1,3-bis(2,6-diisopropylphenyl)-imidazol-2-ylidene resulted in >99% monomer conversion within 30 min, producing polymers with predictable molecular weights and a narrow PDI (1.06). However, the less-hindered and more basic 1,3-diisopropyl-4,5-dimethylimidazol-2-ylidene produced polymers with much broader polydispersities (>2), albeit within a few seconds.

The ROP of cyclic siloxanes and carbosiloxanes catalyzed by NHCs has also been documented. Hedrick, Waymouth and colleagues showed that these organocatalysts would mediate the ROP of 2,2,5,5-tetramethyl-1-oxa-2,5-disilacyclopentane (TMOSC) and hexamethylcyclotrisiloxane (D3) to produce the corresponding ring-opened polymers with a controlled molecular weight and narrow polydispersity (Scheme 14.10) [32].

The ROP of TMOSC resulted in a rapid polymerization (1 min to reach 99% monomer conversion; target DP = 100), although the PDI of the final polymers was slightly broad (1.19). Notably, after complete polymerization the PDIs of the



Scheme 14.10 ROP of 2,2,5,5-tetramethyl-1-oxa-2,5-disilacyclopentane (TMOSC), hexamethylcyclotrisiloxane (D3) and octamethylcyclotetrasiloxane (D4).

NHC-catalyzed polymers were shown to increase (from 1.19 to 1.43), although this loss of control may be attributed to a scrambling of the polymer by silyl ether interchange reactions. An extension of this methodology to the commercially available D3 monomer again resulted in a controlled polymerization. In a separate study, Baceiredo and coworkers showed that the ROP of cyclotetrasiloxane (D4) could be performed efficiently when NHCs were applied as catalysts [33].

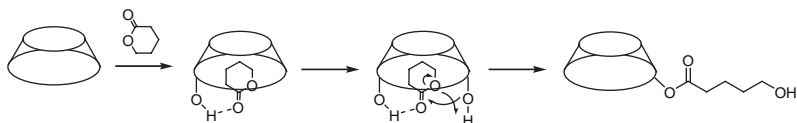
14.2.3

Supramolecular Activation

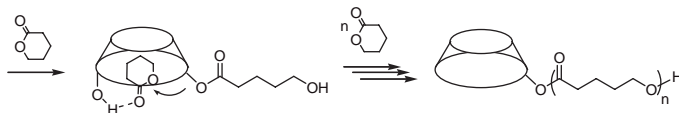
The application of organic compounds capable of mediating the ROP of cyclic ester by supramolecular interactions has provided a new direction for ROP catalysis. In 2004, Harada and coworkers demonstrated the ability of cyclodextrins (CDs) to initiate and mediate the ROP of δ -valerolactone, ϵ -caprolactone and β -butyrolactone in bulk at 100 °C [34]. End-group analysis of the polymers produced by MALDI-ToF and ^1H NMR showed that the CD was acting as both a catalyst and initiator. In the case of δ -valerolactone, γ -CD (i.e. with a larger cavity than β -CD) was also able to efficiently mediate ROP, although a lower yield of polymer was obtained; in both cases an induction period was observed. Examination of the application of α -CD (i.e. a smaller cavity than β -CD) did not result in polymerization occurring. However, in the case of β -butyrolactone ROP, smaller cavities showed higher reactivities, while conversely with ϵ -caprolactone larger cavities more readily produced polymers.

In a later study, the involvement of an inclusion complex was confirmed by the application of free β -CD and the inclusion complexes with δ -valerolactone and adamantane, with the δ -valerolactone inclusion complex eliminating the induction period and adamantane inclusion complex severely retarding ROP [35]. Fourier transform-infrared (FT-IR) studies demonstrated that an appropriate combination of CD and lactone resulted in activation of the lactone in the CD cavity by the formation of a hydrogen bond between the carbonyl oxygen of the lactone and the hydroxyl groups of the CD. Polymerization was proposed to occur without the

Initiation

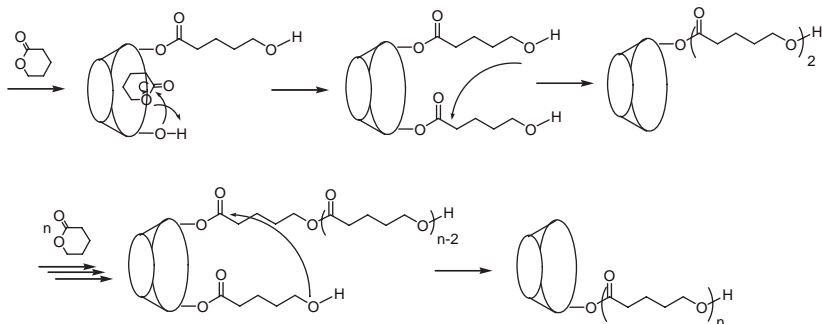


(a)



Propagation

(b)



Scheme 14.11 Proposed mechanism for the ROP of δ -valerolactone by β -cyclodextrin. (Adapted from Ref. [35].)

participation of the alcohol at the chain end, as evidenced by the observation of ROP being mediated by a mono-2-O-(5-benzoyloxypentanoyl)- β -CD (Scheme 14.11). The first step of the polymerization was proposed to be the formation of the lactone inclusion complex with attack from a secondary hydroxyl group at the C2 position of the glucopyranose unit onto the activated carbonyl carbon of the lactone. Propagation was proposed by one of two mechanisms: (i) the insertion of monomer into the terminal ester linkage of the polymer at the CD; and (ii) the formation of a bifunctionalized CD by ring-opening of a second activated lactone and subsequent addition to the chain by attack of the new chain extended alcohol onto the other ester moiety. The disubstituted CDs were not observed by ^1H NMR spectroscopy, which suggested that such a stage occurred rapidly.

Liu, Chen and Fang applied a phthalimide-modified chitosan to synthesize poly(ϵ -caprolactone), both grafted to the phthaloylchitosan and free in solution in the absence of additional catalyst [36]. The application of chitosan and starch under the same conditions did not produce polymer, which suggested that the phthalimido group played an important role in the polymerization. Further investigations applying *N*-butylphthalimide and *N*-benzylphthalimide as catalysts, and benzyl alcohol as an initiator, in the homopolymerization of ϵ -caprolactone led to the production of polymers with predictable molecular weights, narrow polydispersities and end-group fidelity.

Supramolecular activation as a key aspect of ROP was also recently exploited by Hedrick, Waymouth and coworkers. The application of a conjoined bifunctional

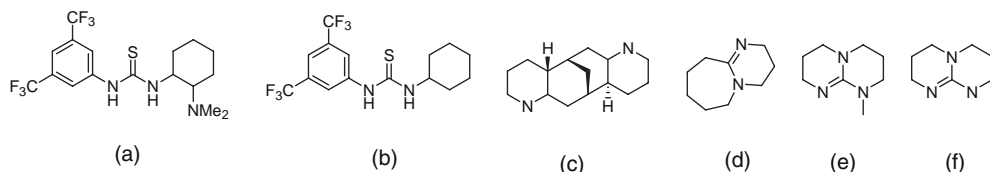
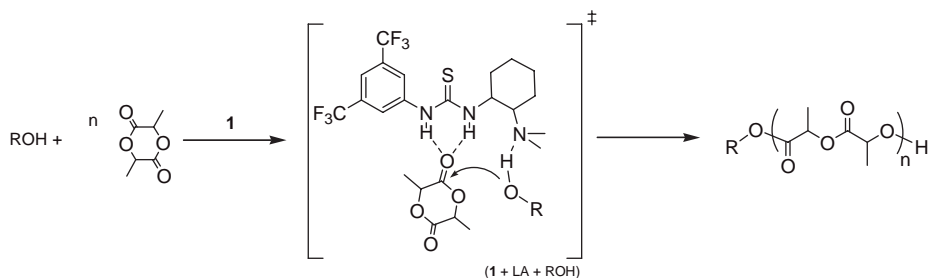


Figure 14.1 Thioureas, amidines and guanidine bases for ROP. (a) Thiourea-amine; (b) 1-cyclohexyl-3-(3,5-bistrifluoromethylphenyl)thiourea; (c) (–)-Sparteine; (d) DBU; (e) MTBD; (f) TBD.

thiourea-tertiary amine compound (Figure 14.1) was shown to be a highly efficient catalyst for the ROP of lactide [37]. The absence of strongly hydrogen-bonding solvents was shown to be essential in order to support ROP, and as such a majority of the studies were carried out as solutions in DCM. The polymerizations demonstrated remarkable control, with the molecular weight increasing in linear fashion with respect to monomer conversion, and corresponding well with the monomer: initiator ratio, producing polymers with narrow polydispersities (<1.08). Although the system required quite high catalyst loadings (up to 10 mol%) and long reaction times to reach high degrees of polymerization, the final polymer product was shown to be remarkably resistant to transesterification.

Studies into the versatility of the system showed that the thiourea and amine moieties were not required to be joined, and the application of separate 1-cyclohexyl-3-(3,5-bistrifluoromethylphenyl)thiourea and *N,N*-dimethylcyclohexylamine resulted in comparable polymerization behavior to that of the unimolecular system being observed. Systematic variation of the phenyl substituents of the thiourea showed that more highly electron-withdrawing units resulted in the highest ROP activity. In further reports [38, 39], it was shown that the polymerization activity could be drastically increased by the application of more strongly basic amines, enabling both more rapid ROP of lactide as well as access to facile ROP of δ -valerolactone and ϵ -caprolactone. The ROP of lactide was found to proceed most efficiently, while maintaining excellent control over the polymerization. Suppression of the transesterification and racemization side reactions was also achieved when applying 1-cyclohexyl-3-(3,5-bistrifluoromethylphenyl)thiourea and (–)-sparteine (Figure 14.1), such that high-DP polymers were obtained within a few hours. It was notable that, even when applying (–)-sparteine (a highly hindered chiral base), the system demonstrated only modest stereoselectivities in the polymerization of *rac*-lactide, with a probability of isotactic enchainment of 0.77 being measured [39].

Despite the increased activity towards the ROP of lactide of the thiourea/sparteine system, a stronger base was required to facilitate the ROP of δ -valerolactone and ϵ -caprolactone [38]. Both 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) or 7-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD) (Figure 14.1), in conjunction with the thiourea, were shown to be highly efficient catalyst systems for the ROP of less-strained monomers, in particular δ -valerolactone. The ROP of this monomer under the conditions applied was shown to proceed rapidly, with



Scheme 14.12 ROP of lactide using unimolecular thiourea–tertiary amine. (Adapted from Ref. [37].)

DP 200 polymers being accessed within 6 h and displaying predictable molecular weights and narrow polydispersities (<1.08). The ROP of ϵ -caprolactone proceeded much more slowly, with DPs in excess of 75 being achieved after five days, albeit with excellent control over the final polymer. In the application of these more active bases, it was found that DBU and MTBD were able to efficiently polymerize lactide in the absence of a thiourea cocatalyst (see Section 14.2.4).

These catalyst systems are proposed to operate by a bifunctional activation mechanism, supported by the absence of ROP when either the thiourea or tertiary amine component is not present. It is proposed that the activation of the carbonyl of the monomer occurs via hydrogen bonding to the thiourea, with concurrent activation of the initiating/propagating alcohol by the basic tertiary amine (Scheme 14.12).

Further mechanistic insights were obtained by nuclear magnetic resonance (NMR) titrations of δ -valerolactone and ϵ -caprolactone into a C_6D_6 solution of thiourea and benzyl alcohol into a C_6D_6 solution of MTBD [38]. In both cases, the resonances attributed to the protons involved in hydrogen bonding displayed a remarkable dependence on the ratio of the two compounds. Notably, the association constants of δ -valerolactone and ϵ -caprolactone with the thiourea at 21 °C were found to be 39 ± 5 and $42 \pm 5 \text{ M}^{-1}$, respectively. However, a comparable experiment in which ethyl acetate was applied as the ester resulted in negligible shifts in the proton resonances involved in hydrogen bonding, indicating a markedly lower binding affinity of the thiourea towards linear esters.

The thiourea–tertiary amine systems have also demonstrated a remarkable efficiency and selectivity in the ROP of TMC [31]. Both, the unimolecular catalyst and the bimolecular thiourea/sparteine system were shown to result in well-controlled polymerizations. As observed in the ROP of lactide, these systems display much lower activities than the NHC-catalyzed reactions, with high monomer conversions being achieved in six days and 12 h, respectively. The molecular weights of the polymers closely matched the predicted molecular weights, while the polydispersities of the resultant polymers were low (1.07–1.09). A further examination of polymerizations mediated by the thiourea/sparteine system showed a linear increase of molecular weight with monomer conversion.

14.2.4

Other Nucleophilic ROP Catalysts

The activation of initiating and propagating alcohols by strong nonionic bases can be utilized to enable the polymerization of strained cyclic ester monomers, such as lactide. As mentioned above, both DBU and MTBD are highly active catalysts for this ROP process, providing DP 500 PLAs within a few minutes at room temperature and 1 mol% catalysts loadings. These amidine and guanidine compounds have comparable pK_a values ($^{\text{MeCN}}pK_{\text{BH}^+} = 24.3$ and 25.4, respectively), and a quasi-anionic polymerization mechanism is proposed [38]. Wade and coworkers reported the application of more highly basic phosphazenes, 2-*tert*-butylimino-2-diethylamino-1,3-dimethylperhydro-1,3,2-diazaphosphorine (BEMP) and *N'*-*tert*-butyl-*N,N,N',N',N',N'*-hexamethylphosphorimidic triamide, *P*₁-*t*-Bu (Figure 14.2), ($^{\text{MeCN}}pK_{\text{BH}^+} = 27.6$ and 26.9, respectively) in the ROP of lactide [40].

The ROP of L-LA in toluene solution (target DP 100) catalyzed by BEMP achieved a 76% conversion within 23 h, producing a well-controlled polymer with $M_n = 13\,100\text{ g mol}^{-1}$ and a narrow PDI (1.08) and end-group fidelity. Further examination of the system showed a linear increase in molecular weight with monomer conversion. The ROP of *rac*-LA resulted in modest stereocontrol at ambient temperature, with a preference for isotacticity ($P_i = 0.70$) being observed. Interestingly, unlike DBU and MTBD, BEMP is able to mediate the ROP of δ -valerolactone and ϵ -caprolactone in the absence of a thiourea cocatalyst. Neat δ -valerolactone was converted to poly(valerolactone) at room temperature, producing a polymer with a predictable molecular weight and narrow PDI (1.12). Again, the ROP of ϵ -caprolactone was dramatically slower, requiring 10 days to reach 14% monomer conversion (target DP 100) at 80°C. An activated alcohol ROP mechanism was proposed in this case (Scheme 14.13).

The application of guanadinium acetate as a catalyst for the ROP of lactides and lactones has also been demonstrated [41, 42]. Polymerization proceeds at 110°C

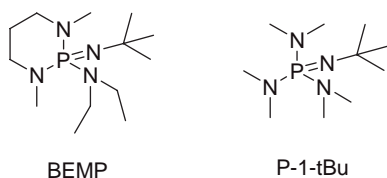
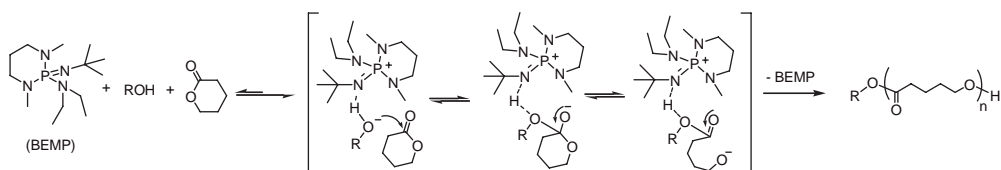
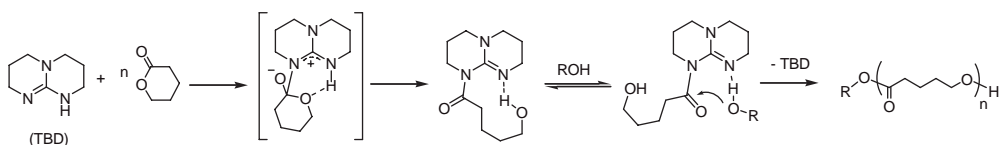


Figure 14.2 Phosphazene bases. BEMP and *P*₁-*t*-Bu. (Adapted from Ref. [40].)



Scheme 14.13 Proposed mechanism for ROP of cyclic esters by BEMP. (Adapted from Ref. [40].)



Scheme 14.14 Proposed mechanism for ROP of cyclic esters by TBD. (Adapted from Ref. [43].)

in bulk in a well-controlled manner, producing polymers with molecular weights comparable to those predicted from the monomer: initiator ratio and with polydispersities below 1.12 [41]. The polymerization was not affected by the addition of NaOH/methanol–toluene or BuOH, which suggested that the ROP was effected via a nonionic mechanism.

In a recent report, Hedrick, Waymouth and coworkers demonstrated the remarkable activity of 1,5,7-triazabicyclo[4.4.0]dec-5-ene (TBD) towards the ROP of cyclic esters [43]. The ROP of L-LA mediated by TBD in CH_2Cl_2 resulted in a rapid polymerization, even with very low catalyst loadings (0.1% relative to monomer), such that a DP 100 PLA could be synthesized within 20 s at room temperature. The polymer produced had $M_n = 24\,200\text{ g mol}^{-1}$ and PDI = 1.19. The control of the polymerization was demonstrated by a linear increase in molecular weight with monomer conversion at a variety of monomer: initiator ratios. Interestingly, the slightly broad PDI was evident at low monomer concentrations, showing this to be the result of a high catalytic activity rather than of transesterification side reactions. TBD was also seen to be a highly active catalyst for the ROP of δ -valerolactone and ϵ -caprolactone, with high conversions in 1.75 M benzene solutions (target DP = 100; 0.5 mol% TBD) being obtained within 30 min and 8 h, respectively. The polymers produced had predictable molecular weights and narrow PDIs. Interestingly, the ROP of ϵ -caprolactone was complicated by transesterification side reactions at higher monomer conversions. A bifunctional polymerization mechanism was proposed in which the nucleophilic attack of the imine nitrogen at the carbonyl of the incoming monomer generated an intermediate in which the adjacent protonated nitrogen of TBD was ideally placed to facilitate proton transfer to the incipient alkoxide to generate the TBD amide. Activation of the incoming initiating/propagating alcohol by hydrogen bonding to the tertiary amine was proposed to result in esterification, thus liberating the chain-extended ester and TBD (Scheme 14.14) [38, 43].

DBU, MTBD and TBD have also shown much promise as catalysts for the ROP of TMC. However, while the guanidine catalysts (TBD and MTBD) produced polymers with molecular weights close to those targeted, the PDIs of the polymers were slightly broad (>1.28). In contrast, the application of DBU to catalyze the ROP resulted in polymers with predictable molecular weights and narrow PDIs (<1.09). Again, end-group fidelity of the polymerization was confirmed by both ^1H NMR and gel-permeation chromatography (GPC), while polymerizations mediated by DBU also showed a linear increase of molecular weight with monomer conversion.

DBU was also shown to be a produce well-controlled polymers (PDI ~ 1.09–1.15) when ROP was performed in bulk at 65 °C.

ROP of the cyclic carbosiloxane, TMOSC (see Scheme 14.10) by TBD resulted in high monomer conversions (target DP = 100) in 6 h. The molecular weight of the polymers produced was shown to correlate well to the monomer: initiator ratio, and to maintain a low PDI throughout the reaction (<1.05). Interestingly, in the case of TBD—and in contrast to the NHC-catalyzed reactions—no silyl ether interchange reactions were detected. This excellent control over ROP of cyclic siloxanes was extended to the commercially available D3 monomer. ROP mediated by TBD resulted in narrowly dispersed polymers (<1.2), again displaying better control than the NHC-catalyzed process (PDI >1.4).

14.3

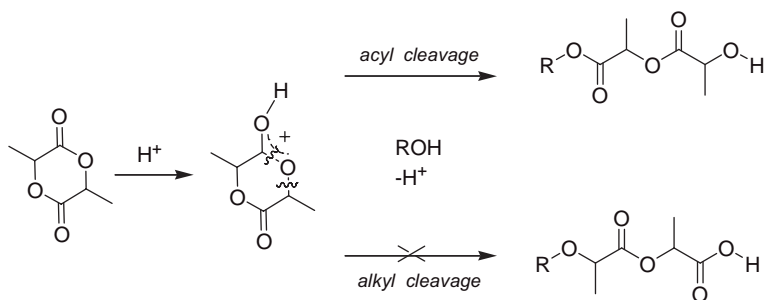
Metal-Free Ionic ROP

14.3.1

Cationic

Several strong mineral and organic acids have been shown to efficiently mediate the controlled cationic ROP of lactide and other cyclic esters. The ROP of ϵ -caprolactone has been reported to occur efficiently when catalyzed by organic acids. Endo and coworkers demonstrated the application of trifluoroacetic and trichloroacetic acids as catalysts for the synthesis of star-shaped poly(ϵ -caprolactone)s in bulk at 70 °C [44]. The polymerizations resulted in polymers with high yields and slightly broad polydispersities (1.67–1.98). The application of sulfonic acid moieties immobilized on silica supports has also been reported to efficiently mediate the ROP of ϵ -caprolactone in toluene solution at 52 °C, producing well-controlled linear polymers [45]. While displaying lower activity than homogeneous *p*-toluenesulfonic acid, the heterogeneous systems resulted in polymers with molecular weights that closely resembled those expected from the monomer: initiator ratio, and with narrow polydispersities (1.10–1.49). HCl·OEt₂ has also been shown to efficiently mediate the ROP of ϵ -caprolactone and δ -valerolactone in CH₂Cl₂ at room temperature and below. The polymerizations displayed several characteristics of a well-controlled polymerization, with the resultant polymers being narrowly disperse (1.02–1.25) [44, 46, 47].

During the 1980s, Kricheldorf and coworkers also demonstrated the cationic ROP of lactide [48, 49]. In more recent study, Bourissou *et al.* showed that the application of trifluoromethanesulfonic acid (triflic acid) was able to efficiently catalyze the ROP of lactide at room temperature in the presence of a protic initiator [50]. The synthesis of PLAs with molecular weights up to 20000 g mol⁻¹ and with relatively narrow polydispersities (<1.5) was demonstrated, with the well-controlled character of the polymerizations being proven by the linear correlation of molecular weight and monomer conversion throughout the polymerization.



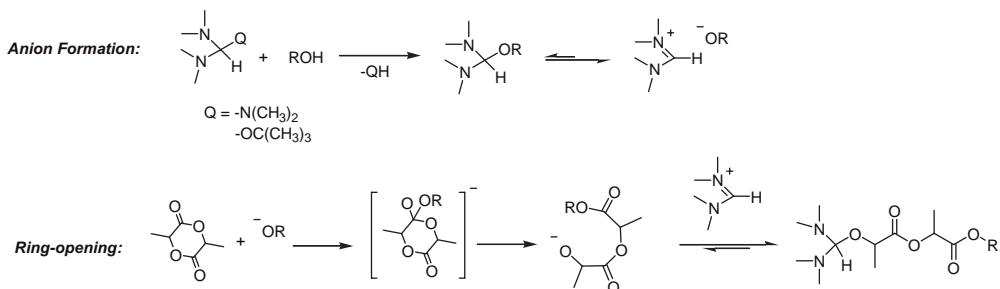
Scheme 14.15 Cationic ROP of lactide. (Adapted from Ref. [50].)

Incorporation of the initiating protic source at the α -chain end of the polymer was confirmed by 1H NMR and mass spectroscopic analysis. The requirement for a strong acid was evidenced by the inactivity towards lactide ROP of trifluoroacetic acid and $HCl \cdot OEt_2$ under comparable conditions. An activated monomer mechanism was proposed in which the protonation of lactide by the acid activated the monomer towards ring opening by nucleophilic addition of the initiating/propagating protic species (Scheme 14.15).

Triflic acid has also been shown to mediate the ROP of β -butyrolactone, producing polymers with predictable molecular weights and low PDIs (<1.12). ROP was shown to occur by acyl–oxygen cleavage and occurred with a retention of stereochemistry [51]. Further investigations revealed that Nafion solid acid catalysts were able to act as catalysts for β -butyrolactone ROP, although difficulties encountered in removing the trace water resulted in the isolation only of oligomers.

The ROP of lactones can also be achieved by the application of much milder organic acids. Several reports have detailed the ROP of ϵ -caprolactone and δ -valerolactone where the polymerization has been catalyzed by additional lactic acid [52, 53], fumaric acid [44], maleic acid [44], tartaric acid [52], citric acid [52] and a range of amino acids [52, 54]. Tartaric acid was shown to be the most active catalyst for the ROP of ϵ -caprolactone in a comparative study performed by Córdova and colleagues [52]. The application of this methodology, in which the polymerizations are carried out in neat lactone at either 120 or 160 $^{\circ}C$, results in the synthesis of polymers with molecular weights that agreed well with the initial monomer: initiator ratio, and with polydispersities ranging from 1.2 to 1.9. Extension to the synthesis of dendrimers such as star poly(ester)s [55] and the polymerization of ϵ -caprolactone from carbohydrates [56] has also been reported.

Organocatalytic cationic polymerization has also been reported for the ROP of TMC and DTC [57–59]. These methods displayed relatively poor control over the polymerization, and were characterized by the incomplete conversion of monomer and broad polydispersities that resulted from extensive back-biting of the polymer chains and decarboxylation. It is worth noting here that the ROP of oxazolines is usually performed by the application of metal-free cations (for an extensive reviewed of this subject, see Chapter 6).



Scheme 14.16 ROP of lactide by latent anionic mechanism, mediated by Bredebeck's reagent. (Adapted from Ref. [60].)

14.3.2

Anionic

In addition to traditional anionic polymerization techniques for the ROP of cyclic esters, the metal-free anionic ROP of lactide has also been reported [60]. Bredebeck's reagent [*tert*-butoxybis(dimethylamino)methane] and related compounds were shown to be latent anionic initiators capable of dissociation to a formamidine cation and an alkoxide anion (Scheme 14.16). These species are then able to propagate PLA formation, resulting in a well-controlled polymerization at 70 °C that produces polymers with predictable molecular weights by monomer conversion and monomer:initiator ratio, with narrow polydispersities (<1.18). Both, NMR and mass spectroscopic investigations have demonstrated incorporation of the alcohol initiator at the end of the polymer chain. The authors proposed that, as a consequence of the electrophilic nature of the formamidine cation counterion, a reversible capture of the propagating anion (Scheme 14.16) was possible, and may be a likely source of the excellent control observed.

14.4

Summary and Prospects

A wide range of metal-free ROPs by catalysts have now been reported and, as a consequence, this area of research is attracting increased interest. Many of the compounds applied are simple (often commercially available) organic acids or bases that often are stable to moisture and oxygen, thus negating the need for complex, air-sensitive manipulations. Moreover, some of these organocatalysts have been found to be extremely active, with imidazolium NHCs and TBD among the most active of those reported to date for the ROP of cyclic esters. Investigations in this field have also led to the discovery of mild catalysts that are compatible with a number of functional groups, and are also highly selective towards ring-opening over transesterification side reactions. Despite this versatility, there remain very few reports of stereochemically controlled ROP mediated by metal-free catalysts;

indeed, until now such control has only been achieved at very low temperatures (below -70°C). However, given the relative youth of this field—in comparison to metal-based catalysis—major developments in this area seem very likely.

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15

Enzyme-Mediated Ring-Opening Polymerization

Andreas Heise, Christopher J. Duxbury, and Anja R. A. Palmans

15.1

Introduction

Enzymes are the catalysts that Nature uses to accelerate biochemical processes in living organisms. Prominent examples of *in vivo* polymer-forming reactions include not only the formation of DNA and proteins, but also the production of polyesters such as poly(hydroxyalkanoates). However, the application of enzymes is not limited to their original environment or natural role. Consequently, enzymes isolated from living organisms have been successfully applied in aqueous and organic media to promote specific reactions, without the need for the entire cell or the organism (*in vitro* catalysis). At present, enzymes are applied in many technical processes on an industrial scale, taking advantage of their chemoselectivity and regioselectivity in order to reduce the number of reaction steps or the enantioselectivity of the enzyme, for example in the synthesis of chiral drug intermediates [1]. Likewise, in polymer chemistry the application of enzymes offers many advantages: polymerizations can be performed under mild conditions with regards to pressure, temperature and pH, which makes enzymatic reactions very energy-efficient. Enzymes can also be highly selective: chemo-, regio- and enantioselectivity can all be enzymatically induced, opening new routes towards precision polymer synthesis. Enzymes are also considered to be ‘green’, nontoxic catalysts, that can meet increasing demands regarding commercial, ecological and biomedical requirements.

Based on the specific reaction that they catalyze, enzymes have been classified into six groups, three of which have been reported to catalyze or induce polymerization *in vitro*, namely oxidoreductases, transferases and hydrolases. The latter class includes lipases, the natural role of which is the hydrolysis of fatty acid esters at the cell’s water–lipid interface. In organic media, lipases can efficiently catalyze ester bond formation, and so have been used extensively in investigations of the *in vitro* synthesis of polyester by polycondensation or ring-opening polymerization (ROP), without the need for any cocatalyst. One enzyme that deserves special attention when discussing enzymatic ROP is *Candida antarctica* Lipase B (CALB).

When physically adsorbed onto macroporous crosslinked beads of poly(methyl methacrylate) (PMMA; Lewatit VP OC 1600, Bayer), this enzyme is available commercially as Novozym 435 from Novozyme [2]. Novozym 435 is a highly versatile catalyst, with activities towards a great variety of different substrates; moreover, the immobilized enzyme is thermostable and retains activity in various organic solvents. Recent breakthroughs in enzymatic ROP are, to a large extent, due to the use of Novozym 435. The success of this material in enzymatic ROP is based partly on its availability and easy handling, which makes it a convenient catalyst—even for chemists with little knowledge of enzymology. Moreover, in many comparative polymerization studies Novozym 435 has been shown to have the highest activity.

In this chapter we provide a brief description of lipase-catalyzed ROP, where we use the word ‘enzyme’ to refer only to lipase. First, we will discuss the specific characteristics of enzymatic ROP, including the mechanistic and kinetic aspects of the reaction. We will then introduce the most important classes of cyclic monomers in enzymatic ROP, after which we will review the use of enzymatic ROP in the synthesis of more complex polymer architectures. For further information, the reader is referred to recent reviews on enzymatic polymerization [3–7].

15.2

Characteristics of Enzymatic ROP

Numerous comparative studies on the ROP of mainly ϵ -caprolactone (CL) in organic solvents have been conducted to enhance the mechanistic and kinetic understanding of enzymatic ROP. The reaction parameters investigated include the enzyme origin [8–12], concentration [13], temperature [14, 15], organic solvent [7, 12, 16, 17] and water content [18, 19]. While a direct comparison of all the reported results is difficult due to the slightly different reaction conditions, a general mechanism and further characteristics can be derived from these studies. Figure 15.1 shows the postulated mechanism for the example of CL as a substrate (monomer). The active site of a lipase comprises a catalytic triad consisting of serine, histidine and aspartate, which are electronically stabilized. The ester moiety of the CL functions as the substrate and undergoes a nucleophilic attack from the primary alcohol group of serine in the enzyme’s active site (stage I in Figure 15.1). Via the enzyme intermediate species (stage II) the original alkoxy-group is released, forming the so-called enzyme-activated monomer (EAM) species (stage III). Subsequently, a nucleophile ($R_2\text{-OH}$) can attack this EAM-species such that, via the new intermediate species (stage IV), the final product is released, thereby regenerating the enzyme. In the propagating step the EAM is attacked nucleophilically by the terminal hydroxy group of a propagating polymer to produce the polymer chain which is extended by one monomer unit. The rate-determining step of the overall polymerization is the formation of the EAM. Thus, the polymerization proceeds via an ‘activated monomer mechanism’, which has the consequence that

Figures and Schemes

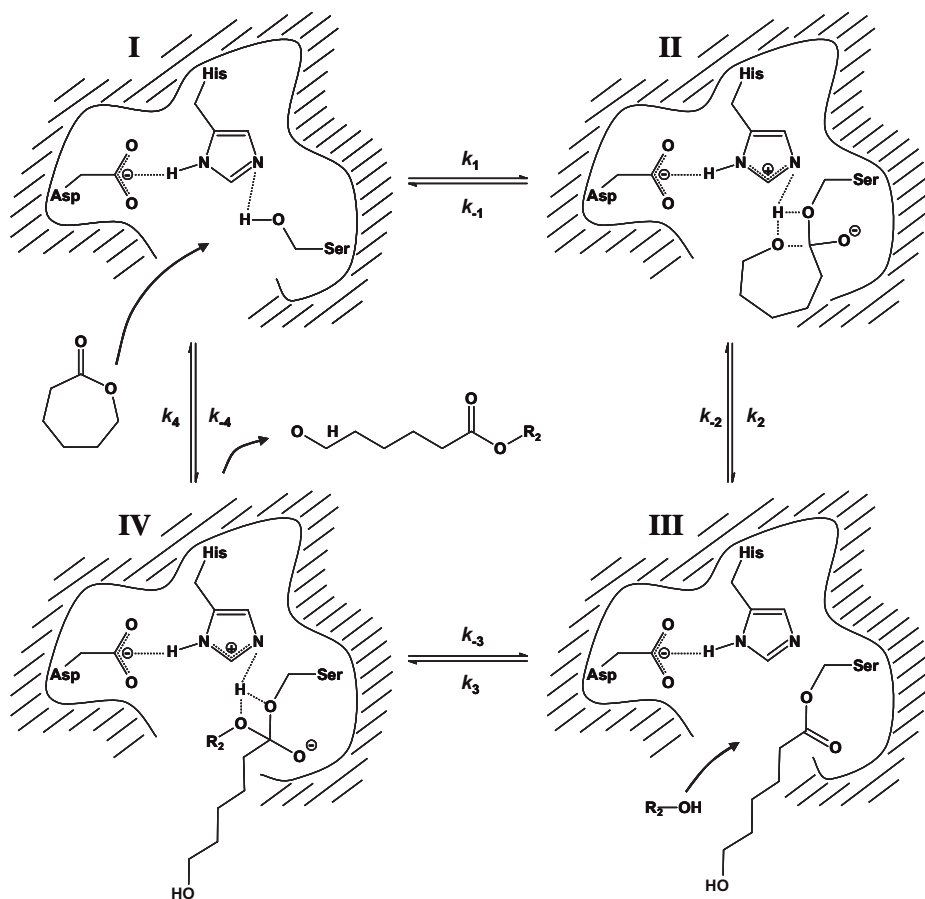


Figure 15.1 Schematic representation of the proposed mechanism of the enzymatic ROP of ϵ -caprolactone.

transesterification reactions occur as the enzyme does not discriminate between ester groups in the monomer and the polymer chain. This leads to chain scission and eventually to equilibration of the structures. Chain scission has also been shown to occur specifically at chain ends with mass selectivity [20, 21]. In the equilibrium position of an enzymatic ROP, one will thus find cyclic and linear polymers in ratios determined by the reaction conditions such as concentration, solvent, temperature and nucleophile concentration and activity. Martinelle and colleagues reported the formation of high concentrations of cyclic polymers of high molecular weights (up to 2600 g mol^{-1}) in the solution polymerization of CL. Whilst up to 53% cyclic polymers was detected by matrix-assisted laser desorption ionization time-of-flight MALDI-ToF spectrometric analysis in acetonitrile, the

concentration was very low in the bulk reaction [12]. A quasi-controlled enzymatic ROP has been reported for the early phase of the reaction (i.e. at low conversion), whereas at higher conversions polycondensation-type reactions occur [16, 22]. In general, the activity of the enzyme is higher the more apolar the reaction medium [23]. The highest conversion rates for a given concentration were thus found in toluene, whereas polar solvents such as dimethylformamide (DMF) or acetonitrile reduce the enzyme activity in enzymatic ROP.

Special attention in this process must be given to the initiation step. In analogy to the metal-mediated ROP of CL (see Chapter 11), the nucleophile ($R_2\text{-OH}$) that is necessary to regenerate the enzyme and create the (ring-opened) product, can be considered as the initiator of the polymerization. This initiator can be water, an alcohol, amine or thiol. While reasonable control over the molecular weight and end-functionalization can be achieved by the addition of a nucleophile, enzymatic ROP does not fulfill the definition of a controlled polymerization due to the presence of transesterification reactions. The initiation by various primary alcohols has been investigated in several studies, ranging from simple mono-alcohols, such as hexanediol or benzylalcohol [18, 24, 25], to more complex polyols such as sugars [26–28] and dendritic structures [29]. The regioselective initiation from only one hydroxyl group was observed. In the case of a functional nucleophile (initiator), functional end groups can be introduced into the polymer chain. Chemoselective initiation was reported by Martinelle and coworkers, using thioalcohols as initiators. Due to the selective initiation of enzymatic ROP from the alcohol group of the initiator, a thiol end-capped poly(ϵ -caprolactone) (PCL) was obtained without protection/deprotection steps [30, 31].

Enzymatic ROP reactions have also been investigated in alternative solvents such as supercritical fluids (SCFs) and ionic liquids. Supercritical carbon dioxide (scCO_2) is the most widely used SCF as it is relatively cheap, readily available and chemically inert. Although scCO_2 is generally a poor solvent for polymers (there are some exceptions to this, such as fluoropolymers and silicones), its ability to plasticize some polymers, such as PCL, has facilitated its use in polymer synthesis and processing. Polymers that neither dissolve nor plasticize in scCO_2 can be solubilized by the introduction of surfactants, stabilizers or cosolvents [32]. The stability of enzymes in SCFs has been investigated, and whilst their effect on enzymes is not completely understood, it has been shown that some enzymes can be stable under supercritical conditions [33]. The use of enzymes as catalysts for ROP in scCO_2 was first investigated in 2001, when Takamoto and colleagues carried out the homopolymerization and copolymerization of CL with 11-undecanolide and 12-dodecanolide, using Novozym 435 [34]. Since this first report, further studies have been conducted to investigate the kinetics of CL ROP, which was found to be similar to reactions in conventional organic solvents, and the use of scCO_2 —not only as a reaction solvent but also as a method of cleaning the high-molecular-weight polymer of low-molecular-weight species and recycling the enzyme catalyst [35, 36].

Ionic liquids represent a popular alternative ‘green’ solvent to SCFs. Very few reports have been made of enzymatic ROP being attempted in ionic liquids,

although the ROP of CL has been successfully carried out using CALB, leading to the formation of relatively low-molecular-weight PCL ($<10\,000\text{ g mol}^{-1}$) [37, 38].

15.3

Classes of Monomer

15.3.1

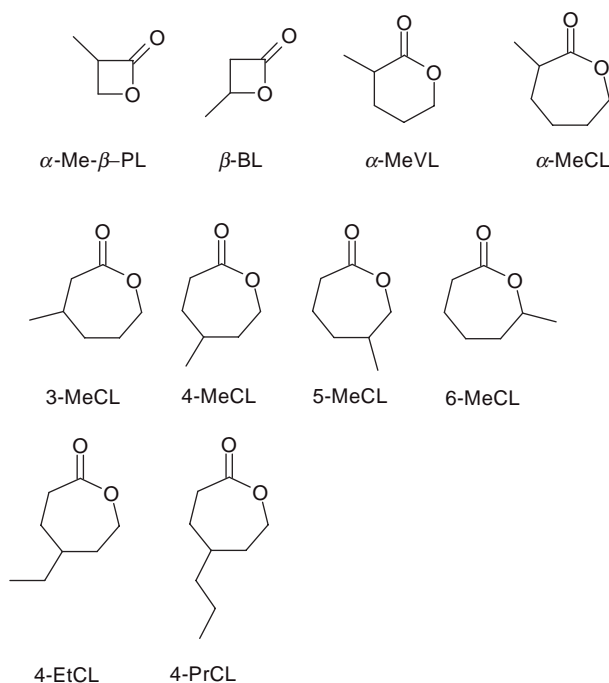
Lactones

Lactones are the most studied class of monomer in enzymatic ROP, of which CL is by far the most investigated. The first *in vitro* example of enzymatic ROP was published in 1993, when Knani *et al.* [39] and Uyama and Kobayashi [40] independently reported the ROP of CL catalyzed by lipases from *Pseudomonas fluorescens* and *Candida cylindracea*, and by porcine pancreatic lipase (PPL). The molecular weight of the obtained PCL was low ($M_n < 2000\text{ g mol}^{-1}$), while the reaction times were long and the polydispersity index (PDI) typically exceeded 5. Since then, the enzymatic ROP of lactones has been intensively studied, and today small-, medium- and large-sized lactones have been found to be efficiently polymerized by lipases. Several reports have been published on the enzymatic ROP of CL, showing that molecular weights between 2000 and $60\,000\text{ g mol}^{-1}$ are readily obtained at elevated temperatures ($60\text{--}90^\circ\text{C}$) in only a few hours using Novozym 435, and with PDIs typically ranging from 1.4 to 3.2. The enzymatic ROP of nonsubstituted lactones has been reported for almost all ring sizes, from four-membered to 17-membered lactones. In contrast to metal-mediated ROP, the macrocyclic lactones have a very high activity in the enzymatic process, and can be polymerized to high molecular weights. (These monomers are discussed in detail in Chapter 11, and so will not be further described here.) Rather, the focus here will be on the enzymatic ROP of substituted lactones as they introduce a unique feature, namely stereoselectivity.

15.3.1.1 Substituted Lactones

The introduction of a substituent at the lactone ring inevitably generates a chiral center. As the action of lipases relies on a two-step mechanism with an acylation step and a deacylation step, involving a covalent acyl-enzyme intermediate (*vide supra*), both the acylation and deacylation step can occur enantioselectively when using a (chiral) substituted lactone [41]. It is well known that lipases such as CALB show a pronounced selectivity for (*R*)-secondary alcohols in the deacylation step [42, 43]. Although less elaborately studied, the acylation step can also occur enantioselectively [44–50], and therefore the enzymatic ROP of substituted lactones may result in optically active polymers, since selectivity for one of the enantiomers can be expected.

Gross and coworkers prepared enantioenriched poly((*R*)- α -methyl- β -propiolactone), making use of the selectivity of lipases. Initially, (*R*)- α -methyl- β -propiolactone (α -Me- β -PL; Scheme 15.1) was isolated via a lipase-catalyzed kinetic



Scheme 15.1 Substituted lactones studied in enzymatic ROP.

resolution, and subsequently chemically polymerized into an optically active polyester [51]. However, the enzymatic ROP of (*rac*)- α -methyl- β -propiolactone using lipase PS-30 from *Pseudomonas fluorescens* afforded a direct route to (*S*)-enriched poly(α -methyl- β -propiolactone) [52]. The enantiomeric ratio (*E* ratio) in toluene was 4.1, and polymers with M_n up to 2900 g mol^{-1} were procured. Marchessault and coworkers investigated the enzymatic ROP of (*rac*)- β -butyrolactone (β -BL; Scheme 15.1) employing PPL and *Pseudomonas cepacia* lipase as the catalyst [53]. Although, the enantioselectivity of the reaction was not evaluated, oligomers with M_n up to 1000 g mol^{-1} were obtained. By using a thermophilic lipase from the ESL-001 CloneZyme library, (*rac*)- β -butyrolactone was polymerized into optically active (*R*)-enriched poly(3-hydroxybutyrate) with an enantiomeric excess (ee) of up to 37% [54]. Wang and coworkers explained the formation of (*R*)-enriched polymers by the rate difference between the reaction of the lipase with the (*R*)- or (*S*)-enantiomer of β -butyrolactone, and/or the rate difference between the reaction of the acyl-enzyme intermediate with (*R*)- or (*S*)-configuration chain ends.

The effect of the substituent position and ring size of the methyl-substituted lactones was studied in detail by Kobayashi and coworkers [5, 6]. Only CALB induced the polymerization of α -methyl substituted δ -valerolactone and CL (α -MeVL and α -MeCL; Scheme 15.1). Both monomers were reactive, but no enantioselection occurred under the reaction conditions employed [55]. Moving the methyl substituent to the ω -position resulted in a low polymerizability of the

substituted lactones when CALB was employed as catalyst. However, the copolymerization of β -butyrolactone with unsubstituted lactones did result in the formation of chiral copolymers, and selectivity for the (*S*)- β -butyrolactone was observed [56, 57]. In the case of the six-membered ring, ω -methyl- δ -valerolactone, a low selectivity for the (*R*)-enantiomer was observed and, again, copolymerizations with unsubstituted lactones were required to obtain polymers of decent molecular weights. Only the 4-methyl-substituted CL showed a polymerizability similar to the unsubstituted CL. A clear indication of the influence of a chiral center far away from the ester bond on polymerization kinetics of enantiomers was found in the enzymatic ROP of (*rac*)-3-methyl-4-oxa-6-hexanolide employing lipase PC as the catalyst (see Scheme 15.1). Here, the initial rate of the (*S*)-enantiomer was sevenfold higher than the initial rate of the (*R*)-enantiomer [58]. Bisht and coworkers studied the enzymatic ROP of 4-methyl- and 4-ethyl-substituted CL (4-MeCL and 4-EtCL; Scheme 15.1) with CALB [59], and in both cases chiral polymers with good molecular weight (M_n up to 5400 g mol^{-1}) and high enantiomeric purity (ee >95%) were obtained, while the (*S*)-enantiomer was found to be the faster-reacting monomer. Finally, the enzymatic ROP of fluorinated lactones with CALB gave optically active products with M_w of $3000\text{--}8000 \text{ g mol}^{-1}$ [60].

Novozym 435, which is CALB immobilized on an acrylic resin, is by far the most widely used biocatalyst in enzymatic ROP. In order to rationalize the selectivity and reactivity of Novozym 435 for substituted caprolactones, a systematic study was conducted of the polymerizability of a range of substituted lactones, where the position and size of the substituent at the CL ring were altered (Scheme 15.1) [61, 62]. The results are summarized in Tables 15.1 and 15.2. CALB showed (*S*)-selectivity for all methyl-substituted CLs, except for 5-MeCL where (*R*)-selectivity was observed. The selectivity was moderate to good, with *E*-ratios varying from 13 to 93. Interestingly, there was an alternating orientation of the methyl group from 3- to 6-MeCL (Figure 15.2), suggesting an odd–even effect. Moreover, 6-MeCL did

Table 15.1 Results of the Novozym 435-catalyzed enzymatic ROP of methyl substituted ϵ -caprolactones.

Monomer	Configuration	k_i (h^{-1}) ^a	Conversion (%) ^a	<i>E</i> -ratio (–)
6-MeCL	6 <i>S</i>	<0.1	4 ^b	n.d.
5-MeCL ^c	5 <i>R</i>	5.0	60 ^d	27 \pm 7
4-MeCL	4 <i>S</i>	1.1	53 ^e	93 \pm 27
3-MeCL ^c	3 <i>S</i>	1.3	12 ^d	13 \pm 4

^a Faster-reacting enantiomer.

^b Reaction stopped after 1.5 h.

^c Data determined from a 1 : 1 mixture of 3- and 5-MeCL.

^d Reaction stopped after 3 h.

^e Reaction stopped after 4 h.

Reaction conditions: benzyl alcohol (0.31 mM) and lactone (15.62 mM) and tetramethylbenzene (TMB) as internal standard were stirred at 45 °C in the presence of Novozym 435 (200 mg).

n.d. = not determined.

Table 15.2 Results of the Novozym 435-catalyzed enzymatic ROP of ϵ -caprolactone (ϵ -CL) and 4-substituted ϵ -caprolactones.

Monomer	Faster-reacting enantiomer	Total conversion (%)	k_i^a (h^{-1})	M_n^b (g mol^{-1})	PD ^b (–)	E-ratio (–)
ϵ -CL	n.a.	>95 ^c	0.684	4100 ^d	2.2 ^d	n.a.
4-MeCL	4S	65 ^c	0.350	6200	2.0	16.9 \pm 2.3
4-EtCL	4S	57 ^c	0.070	4100	2.2	7.1 \pm 0.6
4-PrCL	4R	21 ^e	0.005	1700	1.4	2.0 \pm 0.1

^a Faster-reacting enantiomer.

^b Determined by gel-permeation chromatography, relative to polystyrene standards.

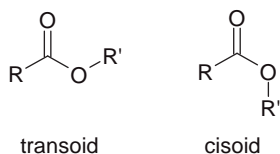
^c After 24 h.

^d Determined at a conversion of 67%.

^e After 72 h.

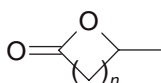
Reaction conditions: benzyl alcohol (0.31 mM) and lactone (15.62 mM) were stirred at 45 °C in the presence of Novozym 435 (200 mg).

n.a. = not applicable.

**Figure 15.2** Cisoid and transoid conformation of the ester bond.

not polymerize under the conditions employed. Although initiation occurred—that is, a ring opening of 6-MeCL with benzyl alcohol—the absence of further consumption of 6-MeCL was indicative of a virtual absence of propagation. This was related to the configuration of the secondary alcohol formed after the ring opening of (*S*)-6-MeCL. Such (*S*)-alcohols are well known to be unreactive in CALB-catalyzed esterifications [40, 63]. Hence, once the lactone ring is opened, an unreactive nucleophile is formed that hardly propagates and hinders the build-up of molecular weight. As (*S*)-6-MeCL is the more reactive lactone in the initiation step (*E*-ratio = 12) [64], polymerization is virtually absent as a result of the formation of an unreactive (*S*)-alcohol chain-end.

By increasing the substituent size at the 4-position of CL, the effect of steric hindrance on the polymerizability of lactones could be evaluated. Novozym 435 is (*S*)-selective for 4-MeCL and 4-EtCL (similar to the results found by Bisht *et al.*), but (*R*)-selective for 4-PrCL. The enantioselectivity rapidly decreases with increasing substituent size. Moreover, the reaction rate dramatically decreases upon going from a methyl to a propyl substituent (see Table 15.2). This suggests that deacylation of the enzyme may be rate-determining in the polymerization of 4-substituted CLs, which is in contrast to the enzymatic ROP of unsubstituted lactones where the acylation step is generally regarded as the rate-determining step [7, 12, 15, 21, 65, 66].



- $n = 1$: β -butyrolactone (β -BL)
 $n = 3$: ω -methyl- δ -valerolactone (5-MeVL)
 $n = 4$: ω -methyl- ϵ -caprolactone (6-MeCL)
 $n = 5$: ω -methyl-7-heptanolactone (7-MeHL)
 $n = 6$: ω -methyl-8-octanolactone (8-MeOL)
 $n = 10$: ω -methyl-12-dodecanolactone (12-MeDDL)

Scheme 15.2 Racemic methylated lactones employed in these studies.

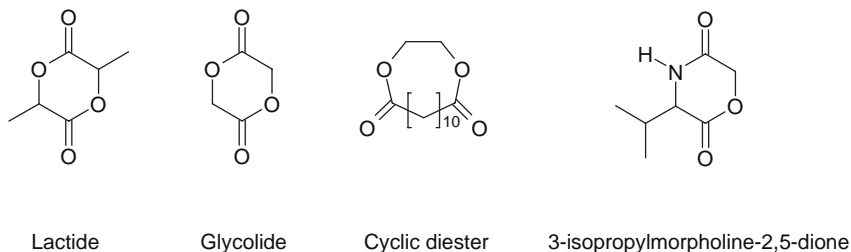
Table 15.3 Selectivity of Novozym 435 for ω -methylated lactones.^a

Monomer	Selectivity	k_{cat} (1 s ⁻¹)	
		S-enantiomer	R-enantiomer
β -BL	S	45.7	n.d. ^b
5-MeVL ^c	— ^d	7.9	7.6
6-MeCL	S	49.3	8.5
7-MeHL	R	0.01 ^e	204.4
8-MeOL	R	n.d. ^b	10.3
12-MeDDL ^f	R	n.d. ^b	23.3

- a Reaction conditions: lactone (4 mM), BA (1 mM), Novozym 435 (27 mg), 1,3,5-tri-*t*-butylbenzene (0.3 mM, internal standard) in toluene (2 ml); reaction conducted at 70 °C.
 b Could not be determined.
 c Experiment performed with excess of 1-octanol (8 mM) as initiator because of ring-chain equilibrium; enzyme dried overnight at 50 °C over P2O5.
 d No significant enantioselectivity was observed for the reaction.
 e Determined in a separate experiment using 2 mM isolated (S)-7-MeHL.
 f 2 mM 12-MeDDL.

Because of the fascinating opposite selectivity of Novozym 435 for acyl donor and alcohol nucleophile in the case of 6-MeCL, this investigation was extended to ω -methylated lactones of different ring sizes. Several ω -methylated lactones, from a four- to a 13-membered ring, were synthesized in their racemic forms (Scheme 15.2) and subjected to Novozym 435-catalyzed ring opening employing benzyl alcohol (BA) as the nucleophile [67]. The results are summarized in Table 15.3.

The data in Table 15.3 show fascinating differences in the selectivities and reaction rates of the ring opening of the different lactones with Novozym 435. The differences appear to be related to the conformation of the ester in the lactone (see Figure 15.2), which can exist in either the higher-energy *cisoid* conformation or the lower-energy *transoid* conformation [68–70]. Up to the seven-membered ring (CL), only the *cisoid* conformation of the ester bond is possible; however, starting from the eight-membered ring the *transoid* conformation becomes possible, while from the 10-membered ring onwards the ester bond is exclusively in the *transoid* conformation. Whilst ring opening of the small lactones that are exclusively in a *cisoid* conformation is (S)-selective (β -BL and 6-MeCL) or nonselective (5-MeVL), ring opening of the lactones that can adopt a *transoid* conformation (7-MeHL,



Scheme 15.3 Chemical structure of lactide, glycolide, cyclic diesters and cyclic ester amide.

8-MeOL, 12-MeDDL) is exclusively (*R*)-selective. The change in selectivity is abrupt: while Novozym 435 is moderately selective for (*S*)-6-MeCL, almost complete enantioselectivity is observed for the (*R*)-enantiomer in 7-MeHL. The reactivity of the faster-reacting enantiomers of the different lactones also varies quite significantly. The relative reactivities are similar to the relative reactivities found previously for the ROP of unsubstituted lactones [71]. For the higher-membered ring lactones, on the other hand, the (*R*)-lactone is the preferred substrate (see Table 15.3). As a consequence, ring opening affords an (*R*)-terminal alcohol, which is accepted as the nucleophile. Indeed, Novozym 435 catalyzes the ROP of 7-MeHL, 8-MeOL and 12-MeDDL, furnishing the corresponding (*R*)-polyesters and the unreacted (*S*)-lactones.

15.3.2

Lactides/Glycolide/Depsipeptides and Cyclic Diesters

In addition to cyclic lactones, cyclic diesters and cyclic ester amides can also be used as monomers in enzymatic ROP. An overview of monomers evaluated is provided in Scheme 15.3.

Lactide is the cyclic dimer of lactic acid, and can occur in three stereoconfigurations: L,L-lactide, D,D-lactide and D,L-lactide (see also Chapter 10). By analogy, glycolide is the cyclic dimer of glycolic acid, but is achiral as it lacks a chiral center. Both, lactides and glycolide are highly reactive in chemical ROP and afford biocompatible and biodegradable polymers that are used in a variety of biomedical applications. Consequently, both monomers have attracted interest in the exploration of enzymatic ROP.

The reactivity of lactic acid as an acyl donor and an alcohol nucleophile was investigated in detail by Adlercreutz and coworkers [72]. The esterification of lactic acid with a variety of alcohols in hexane was very promising when employing Novozym 435 as the biocatalyst. Moreover, it was found that in the esterification of (*rac*)-lactic acid, both enantiomers showed similar reactivity, which suggested that CALB is not enantioselective when the substituent is placed at the carbonyl side. Interestingly, no formation of lactic acid oligomers was observed, even if an excess of lactic acid was used, suggesting that the secondary alcohol is rather unreactive. This was corroborated when fatty acids were employed as acyl donor in an esterification of lactic acid, and no ester formation was observed. Apparently,

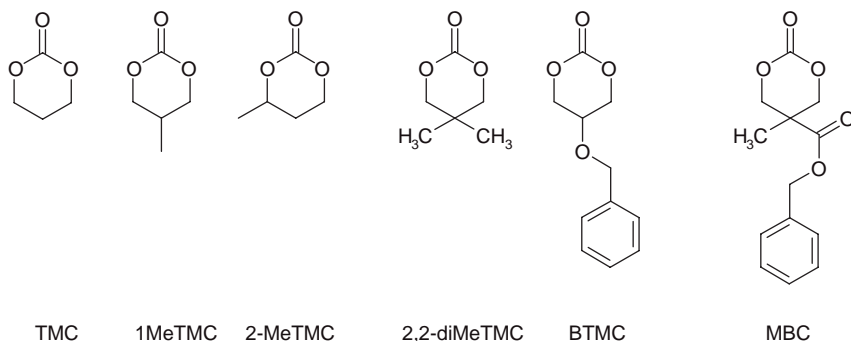
the carbonyl group provides additional steric hindrance, thus dramatically limiting the reactivity of the secondary alcohol in lactic acid. However, over a longer time scale an esterification of lactic acid with caprylic acid in hexane was observed when using Novozym 435, although the yields were low and the reaction times high (30% conversion in four days) [73].

The lack of reactivity of the alcohol moiety of lactic acid when using Novozym 435 as catalyst would imply that lactide is not a good substrate in enzymatic ROP, as propagation requires an active chain end. Indeed, copolymerizations of lactide with CL showed a dramatic decrease in CL consumption after an initial rapid consumption of lactide, which appeared to be the better substrate. Indeed, many weeks were required in order to observe the formation of random copolymers [74]. Clearly, the lack of nucleophilicity of the secondary alcohol of ring-opened lactide is primarily responsible for the dramatic reduction in polymerization rate.

Subsequently, changing to lipase PS did allow for the enzymatic ROP of lactide, when Matsumura and coworkers reported the creation of polymers with extraordinary high molecular weights (M_w up to $270\,000\text{ g mol}^{-1}$) and very narrow PDI values (<1.3) [75, 76]. However, high temperatures (130°C) were needed to achieve good conversions, and the polymerizations proceeded only when conducted in bulk. Endo and coworkers recently demonstrated the ROP of CL in bulk at high temperature using an insoluble acid, such as fumaric acid, as the catalyst. Polyesters of high M_w and narrow PDI could be obtained in this way [77]. It is conceivable that, in the enzymatic ROP of lactide, this cationic mechanism also played a role, as lactic acid is a common impurity in lactide. In fact, Koning and coworkers synthesized copolymers of glycolide and lactide using immobilized *Pseudomonas cepacia* lipase, and highlighted the possibility of a cationic mechanism being operational during the enzymatic polymerization [78]. Clearly, further studies are required here to clarify the exact mechanism of enzymatic ROP of lactides.

Despite the fact that glycolic acid has been successfully used as an acyl donor in esterification reactions with fatty alcohols, few reports exist describing the enzymatic ROP of glycolides [79]. On the other hand, cyclic diesters based on ethylene glycol have been polymerized successfully by lipase catalysis and have afforded AA-BB-type polyesters [80]. As macrocyclic lactones are better substrates than small lactones, it can be expected that a wide range of macrocyclic diesters are suitable monomers for enzymatic ROP.

Cyclic depsipeptides such as 3-isopropylmorpholine-2,5-dione (see Scheme 15.3) are interesting monomers for the synthesis of polyesteramides. Höcker and coworkers investigated the enzymatic ROP of 3-isopropylmorpholine-2,5-dione and other derivatives in detail, employing lipases of different origin as the catalyst [81–83]. Several lipases (PPL, PS), with the exception of Novozym 435, catalyzed the polymerization reaction, but high temperatures ($100\text{--}130^\circ\text{C}$) and bulk conditions were required. The final M_n values ranged from 3500 to $12\,000\text{ g mol}^{-1}$. During the polymerization of optically pure 3(*S*)-isopropylmorpholine-2,5-dione, racemization took place at the valine residue in the polymer, and the polyesteramides obtained were optically inactive.



Scheme 15.4 Substituted and unsubstituted cyclic carbonates used in enzymatic ROP.

15.3.3

Cyclic Carbonates and Cyclic Phosphates

Cyclic carbonates are an interesting class of monomers, since polycarbonates such as poly(trimethylene carbonate) are often amorphous and show well-defined degradation properties, making them suitable for a variety of biomedical applications [84, 85]. The ROP of cyclic carbonates is typically conducted with metal-based catalysts such as $\text{Sn}(\text{Oct})_2$ (see Chapter 12), although lipases were also found to be active in the enzymatic ROP of a variety of substituted and unsubstituted cyclic carbonates (Scheme 15.4). Trimethylenecarbonate (TMC) was the first monomer to be evaluated in enzymatic ROP [86–88]. Here, Novozym 435 provided a rapid polymerization reaction, with an M_n of $15\,000\text{ g mol}^{-1}$ being reached with quantitative monomer conversion within 120 h at 70°C [85]. Higher molecular weights have been reached by using lipase PPL immobilized on silica nanoparticles, although this required a temperature of 100°C [89]. By using such high temperatures, the spontaneous polymerization of TMC cannot be excluded, since Kricheldorf and colleagues showed that TMC could be polymerized up to a high M_n of $65\,000\text{ g mol}^{-1}$ with yields of 90% in bulk at 100°C , presumably via an anionic mechanism [90].

The ability of lipases to catalyze not only ROPs but also transesterification/transacylation reactions was exploited by preparing random copolymers of TMC with CL or ω -pentadecalactone, and copolymers of cyclic dicarbonates with CL and 12-dodecanolactone [91–94]. The introduction of substituents at the cyclic carbonate (1-MeTMC and 2-MeTMC; Scheme 15.4) has also been studied, and their homopolymers and copolymers with TMC have been prepared [95–99]. The use of protected functional groups at the TMC ring (BTMC and MBM; Scheme 15.4) allowed for easy access to the hydroxy-functional or carboxy-functional polycarbonates, which may be used to tune the degradation behavior of these polymers.

The synthesis of polyphosphates—which form an interesting class of biocompatible and biodegradable polymer—from ethylene phosphate and ethylene isobutyl phosphate, was studied using PPL by Zhuo and coworkers [95, 100]. Although the

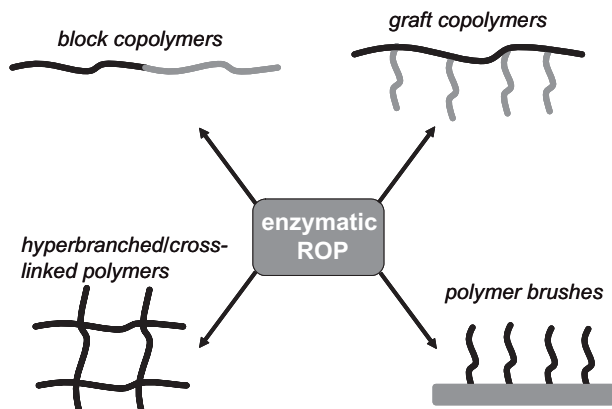


Figure 15.3 Polymer architectures reported from enzymatic ROP.

results were encouraging, with polymers of M_n up to 5800 g mol^{-1} being reported, the isolated yields were only moderate and high reaction temperatures were required (120°C to limit the reaction times to 24–48 h).

15.4

Polymer Architectures Employing Enzymatic ROP

Today, enzymatic ROP is increasingly being investigated for the production not only of simple linear homopolymers and copolymers, but also of more complex polymer architectures (Figure 15.3). The goal of this line of research is to: (i) develop an understanding of the scope and limitations of enzymatic ROP in the synthesis of complex structures; and (ii) create materials which are unavailable from chemical catalysis by taking advantage of the unique selectivity of enzymes.

15.4.1

Block Copolymers

The synthesis of block copolymers by the enzymatic macroinitiation of lactones was reported following two strategies: enzymatic ROPs from chemically obtained macroinitiators; and macroinitiation from functional polymers obtained from enzymatic ROPs. By following the first approach, Gross and Hillmyer reported the initiation of CL and pentadecalactone by Novozym 435 from hydroxyl functional polybutadiene of various molecular weights ($2600\text{--}19\,000 \text{ g mol}^{-1}$) with an initiation efficiency of $>90\%$ to yield the respective block copolymers [101]. Poly(ethylene glycol) (PEG)-based diblock and triblock copolymers were prepared, using a similar approach, from the corresponding hydroxyl functionalized PEG macroinitiators by Feng He *et al.* [102] with CL, and by Srivastava and Albertsson [103] with CL and 1,5-dioxepane-2-one (DXO).

By following the second strategy, Heise and Palmans used bifunctional initiators carrying an hydroxyl group for enzymatic ROP and a group capable of controlled radical polymerization, such as nitroxide-mediated polymerization (NMP) and atom transfer radical polymerization (ATRP) [18, 58, 104, 105]. Careful optimization of the reaction conditions and the ATRP initiator structure resulted in a high yield of macroinitiator; then, by subsequent ATRP of methyl methacrylate (MMA), P(CL-*b*-MMA) was obtained. While it was not possible to conduct both reactions in one pot, due to the inhibiting effect of the ATRP metal catalyst on the lipase, block copolymer synthesis combining enzymatic ROP and NMP of styrene (St) was possible with intermediate work-up in one pot. P(CL-*b*-St), and the production of chiral block copolymers comprising a poly((*S*)-4-methyl CL) block was reported. Kerep and Ritter also described the synthesis of P(CL-*b*-St) by enzymatic ROP of CL with 2-mercaptoethanol as the initiator, both in an oil bath and under microwave irradiation. Due to the chemoselectivity of the enzyme, however, PCL with predominantly thiol end-groups were obtained, and these were subsequently used as a macroinitiator for St [106].

Enzymatic ROP has also been successfully combined with chemically catalyzed polymerization methods in scCO₂, allowing the formation of block structures. For example, Howdle and coworkers reported a simultaneous use of Novozym 435 with metal-catalyzed ATRP that allowed the formation of block copolymers of PCL and PMMA [107, 108], whilst a two-step methodology was used to form block copolymers of PCL with poly(fluoro-octyl methacrylates) (PFOMA) [109]. Similar reactions, simultaneously combining reversible addition–fragmentation chain transfer (RAFT) with enzymatic ROP to form block copolymers of polystyrene and PCL, have also been performed in scCO₂ [110]. Block copolymer synthesis in scCO₂ has recently been reviewed [111].

15.4.2

Graft Copolymers

In analogy to the block copolymers, graft copolymers have been obtained by two strategies. Gross and colleagues reported the enzymatic ROP of PDL in the presence of hydroxyl ethyl methacrylate (HEMA) and α -hydroxyl- ω -methacrylate-poly(ethylene glycol) (PEGMA; M_n 360 g mol⁻¹) to form an acrylate end-capped PPDL. The subsequent free-radical polymerization of the macromonomer yielded highly crystalline graft copolymers [112]. Albertsson and coworkers described a similar approach for the HEMA initiation of CL and DXO, followed by free-radical polymerization [113]. Alternatively, the synthesis of graft copolymers was achieved by enzymatic ROP from linear multifunctional polymer backbones. In a systematic study, Moeller and colleagues compared the enzymatic and chemical grafting of CL from linear and star-shaped polyglycidol, and found that a maximum of 20% of the hydroxyl groups reacted in the enzymatic grafting process [114]. Later, Heise and coworkers investigated the enzymatic ROP from poly(styrene-*co*-4-vinylbenzyl alcohol), for which a maximum of 60% reacted hydroxyl groups was found [115]. As in these reactions carried out in conventional solvents, grafting conducted in

scCO₂ from P(HEMA-*co*-PMMA) did not occur from all of the hydroxyl groups on the polymeric initiator. In all cases, steric effects were suggested to be responsible for the incomplete grafting reaction [116].

A surface-initiated enzymatic ROP has also been reported, whereby CL and DXO were grafted from hydroxyl-terminated self-assembled monolayers (SAMs) on gold, using Novozym 435 [117], while polycaprolactone-modified hydroxyethylcellulose films were prepared by the enzymatic ROP of CL [118].

15.4.3

Branched and Crosslinked Polymers

Branched structures by enzymatic ROP were reported by Frey and coworkers, who followed the classical approach of polymerizing CL in the presence of an ABIX₂ monomer, namely 2,2-bis(hydroxymethyl)butyric acid. As a consequence, polymers with a degree of branching of up to 0.33 were reported [119]. In another report, heterotelechelic PCL macroinimer was synthesized in a one-pot enzymatic procedure by using 2-hydroxyethyl α -bromoisobutyrate as a bifunctional initiator. A polymerizable end group was introduced by subsequent *in situ* enzymatic acrylation with vinyl acrylate. The synthesis of branched polymers by self-condensing ATRP of the macroinimers was successfully conducted, with and without the addition of MMA as a comonomer [120].

15.5

Summary and Prospects

In recent years, enzymatic polymerization has found its place within the ‘toolbox’ of synthetic methods, with much research having been conducted to raise the level of understanding of this young technology to that of traditional polymerization techniques. Nowhere is this situation more prominent than in the lipase-catalyzed ROP of cyclic monomers. Contributions to the fundamental kinetic and mechanistic understanding are increasingly complemented by the development of novel materials and polymer architectures, and this has led to a situation where the enzymatic ROP can be compared directly to its chemical counterpart, and its specific characteristics and advantages identified.

The unique nature of enzymatic polymerization lies in the fact that it covers the interface between the biological and the material worlds. The availability of a stable, robust lipase formulation (such as Novozym 435) can be considered an important stepping-stone to bridge both worlds, as it not only allows polymer chemists to apply enzymatic ROP without a deep knowledge of enzymology or biotechnology, but also represents a unique opportunity for the future design of novel functional materials. Questions remain, however, as to whether we can use the selectivity of enzymes to produce materials unavailable by chemical synthesis? Likewise, can natural concepts such as chirality be applied to materials science? Clearly, such questions must be addressed to determine the future impact of

enzymatic polymerization in general, and enzymatic ROP in particular. Hopefully, this chapter has provided a first impression of research activities in that direction.

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